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(54) Title: NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN FAMILY AND USES THEREOF

(57) Abstract

Novel Tango-77 polypeptides, proteins, and nucleic acid molecules are disclosed. In addition to isolated, full-length Tango-77 proteins, the invention further provides isolated Tango-77 fusion proteins, antigenic peptides and anti-Tango-77 antibodies. The invention also provides Tango-77 nucleic acid molecules, recombinant expression vectors containing a nucleic acid molecule of the invention, host cells into which the expression vectors have been introduced and non-human transgenic animals in which a Tango-77 gene has been introduced or disrupted. Diagnostic, screening and therapeutic methods utilizing compositions of the invention are also provided.

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- 1 -

NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN
FAMILY AND USES THEREOF

Background of the Invention

The polypeptide cytokine interleukin-1 (IL-1) 5 is a critical mediator of inflammatory and overall immune response. To date, three members of the IL-1 family, IL-1 α , IL-1 β and IL-1ra (Interleukin-1 receptor antagonist) have been isolated and cloned. IL-1 α and IL-1 β are proinflammatory cytokines which elicit 10 biological responses, whereas IL-1ra is an antagonist of IL-1 α and IL-1 β activity. Two distinct cell-surface receptors have been identified for these ligands, the type I IL-1 receptor (IL-1R tI) and type II IL-1 receptor (IL-1R tII). Recent results suggest that the IL-1R tI is 15 the receptor responsible for transducing a signal and producing biological effects.

As mentioned above, IL-1 is a key mediator of the host inflammatory response. While inflammation is an important homeostatic mechanism, aberrant inflammation 20 has the potential for inducing damage to the host. Elevated IL-1 levels are known to be associated with a number of diseases particularly autoimmune diseases and inflammatory disorders.

Since IL-1ra is a naturally occurring inhibitor of 25 IL-1, IL-1ra can be used to limit the aberrant and potentially deleterious effects of IL-1. In experimental animals, pretreatment with IL-1ra has been shown to prevent death resulting from lipopolysaccharide-induced sepsis. The relative absence of IL-1ra has also been 30 suggested to play a role in human inflammatory bowel disease.

Summary of the Invention

The present invention is based, at least in part, on the discovery of a gene encoding Tango-77, a secreted

- 2 -

protein that is predicted to be a member of the cytokine superfamily. The Tango-77 cDNA described below (SEQ ID NO:1) has three possible open reading frames. The first potential open reading frame encompasses 534 nucleotides 5 extending from nucleotide 356 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from about amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second potential open reading frame encompasses 498 nucleotides extending from nucleotide 389 15 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein may include a predicted signal sequence of about 52 amino acids (from about amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted 20 mature protein of about 115 amino acids (from about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third potential open reading frame encompasses 408 nucleotides extending from nucleotide 481 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:10) and encodes 25 a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from about amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

As used herein, the terms "Tango-77", "Tango-77 protein", "Tango-77 polypeptide" and the like, can refer and polypeptide produced by the cDNA of SEQ ID NO:1 including any and all of the Tango-77 gene products 35 described above.

- 3 -

Tango-77 is expected to inhibit inflammation and play a functional role similar to that of secreted IL-1ra. For example, it is expected that Tango-77 may bind to the IL-1 receptor, thus blocking receptor activation by inhibiting the binding of IL-1 α and IL-1 β to the receptor. Alternatively, Tango-77 may inhibit inflammation through another pathway, for example, by binding to a novel receptor. Accordingly, Tango-77 may be useful as a modulating agent in regulating a variety of cellular processes including acute and chronic inflammation, e.g., asthma, chronic myelogenous leukemia, rheumatoid arthritis, psoriasis and inflammatory bowel disease.

In one aspect, the invention provides isolated nucleic acid molecules encoding Tango-77 or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection of Tango-77.

The invention encompasses methods of diagnosing and treating patients who are suffering from a disorder associated with an abnormal level (undesirably high or undesirably low) of inflammation, abnormal activity of the IL-1 receptor complex, or abnormal activity of IL-1, by administering a compound that modulates the expression of Tango-77 (at the DNA, mRNA or protein level, e.g., by altering mRNA splicing) or by altering the activity of Tango-77. Examples of such compounds include small molecules, antisense nucleic acid molecules, ribozymes, and polypeptides.

The invention features a nucleic acid molecule which is at least 45% (e.g., 55%, 65%, 75%, 85%, 95%, or 98%) identical to the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA insert of the plasmid

- 4 -

deposited with ATCC as Accession Number (the "cDNA of ATCC 98807"), or a complement thereof.

The invention features a nucleic acid molecule which includes a fragment of at least 100 (e.g., 250, 5 325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989) nucleotides of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA ATCC 98807, or a complement thereof.

10 The invention also features a nucleic acid molecule which includes a nucleotide sequence encoding a protein having an amino acid sequence that is at least 45% (55%, 65%, 75%, 85%, 95%, or 98%) identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID 15 NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, or the amino acid sequence encoded by the cDNA of ATCC 98807.

In a preferred embodiment, a Tango-77 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the 20 nucleotide sequence of the cDNA of ATCC 98807.

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID 25 NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment includes at least 15 (e.g., 25, 30, 50, 100, 150, or 178) contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide 30 encoded by the cDNA of ATCC Accession Number 98807.

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, 35 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or

- 5 -

an amino acid sequence encoded by the cDNA of ATCC Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or a 5 complement thereof under stringent conditions.

Also within the invention are: an isolated Tango-77 protein having an amino acid sequence that is at least about 45%, preferably 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:5, SEQ 10 ID NO:9 or SEQ ID NO:13 (mature human Tango-77), or the amino acid sequence of SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11 (immature human Tango-77).

Also within the invention are: an isolated Tango-77 protein which is encoded by a nucleic acid 15 molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807; and an isolated Tango-77 protein which is encoded by a nucleic acid molecule having a nucleotide sequence 20 which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the non-coding strand of the cDNA of ATCC 98807, or the complement thereof.

25 Also within the invention is a polypeptide which is a naturally occurring allelic variant of a polypeptide that includes the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an 30 amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID

- 6 -

NO:10 or the complement thereof under stringent conditions.

Another embodiment of the invention features Tango-77 nucleic acid molecules which specifically detect

5 Tango-77 nucleic acid molecules relative to nucleic acid molecules encoding other members of the cytokine superfamily. For example, in one embodiment, a Tango-77 nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule comprising the

10 nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In another embodiment, the Tango-77 nucleic acid molecule is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989)

15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In yet another embodiment, the

20 invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a Tango-77 nucleic acid.

Another aspect of the invention provides a vector, e.g., a recombinant expression vector, comprising a

25 Tango-77 nucleic acid molecule of the invention. In another embodiment, the invention provides a host cell containing such a vector. The invention also provides a method for producing Tango-77 protein by culturing, in a suitable medium, a host cell of the invention containing

30 a recombinant expression vector such that a Tango-77 protein is produced.

Another aspect of this invention features isolated or recombinant Tango-77 proteins and polypeptides. Preferred Tango-77 proteins and polypeptides possess at

35 least one biological activity possessed by naturally

- 7 -

occurring human Tango-77, e.g., (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an 5 intracellular target protein, (iv) the ability to interact with a protein involved in inflammation and (v) the ability to bind the IL-1 receptor. Other activities include the induction and suppression of polypeptide interleukins, cytokines and growth factors.

10 The Tango-77 proteins of the present invention, or biologically active portions thereof, can be operably linked to a non-Tango-77 polypeptide (e.g., heterologous amino acid sequences) to form Tango-77 fusion proteins. The invention further features antibodies that 15 specifically bind Tango-77 proteins, such as monoclonal or polyclonal antibodies. In addition, the Tango-77 proteins or biologically active portions thereof can be incorporated into pharmaceutical compositions, which optionally include pharmaceutically acceptable carriers.

20 In another aspect, the present invention provides a method for detecting the presence of Tango-77 activity or expression in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of Tango-77 activity or expression such that 25 the presence of Tango-77 activity or expression is detected in the biological sample.

In another aspect, the invention provides a method for modulating Tango-77 activity comprising contacting a cell with an agent that modulates (inhibits or 30 stimulates)

Tango-77 activity or expression such that Tango-77 activity or expression in the cell is modulated. In one embodiment, the agent is an antibody that specifically binds to Tango-77 protein. In another embodiment, the

agent modulates expression of Tango-77 by modulating transcription of a Tango-77 gene, splicing of a Tango-77 mRNA, or translation of a Tango-77 mRNA. In yet another embodiment, the agent is a nucleic acid molecule having a 5 nucleotide sequence that is antisense to the coding strand of the Tango-77 mRNA or the Tango-77 gene.

In one embodiment, the methods of the present invention are used to treat a subject having a disorder characterized by aberrant Tango-77 protein activity or 10 nucleic acid expression by administering an agent which is a Tango-77 modulator to the subject. In one embodiment, the Tango-77 modulator is a Tango-77 protein. In another embodiment, the Tango-77 modulator is a Tango-77 nucleic acid molecule. In other embodiments, 15 the Tango-77 modulator is a peptide, peptidomimetic, or other small molecule. In a preferred embodiment, the disorder characterized by aberrant Tango-77 protein or nucleic acid expression can include chronic and acute inflammation.

20 The present invention also provides a diagnostic assay for identifying the presence or absence of a genetic lesion or mutation characterized by at least one of: (i) aberrant modification or mutation of a gene encoding a Tango-77 protein; (ii) mis-regulation of a 25 gene encoding a Tango-77 protein; and (iii) aberrant post-translational modification of a Tango-77 protein, wherein a wild-type form of the gene encodes a protein with a Tango-77 activity.

In another aspect, the invention provides a 30 method for identifying a compound that binds to or modulates the activity of a Tango-77 protein. In general, such methods entail measuring a biological activity of a Tango-77 protein in the presence and absence of a test compound and identifying those

- 9 -

compounds which alter the activity of the Tango-77 protein.

The invention also features methods for identifying a compound which modulates the expression of 5 Tango-77 by measuring the expression of Tango-77 in the presence and absence of a compound.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

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Brief Description of the Drawings

Figure 1 depicts the cDNA sequence (SEQ ID NO:1) of Tango-77. The Tango-77 cDNA has three possible open reading frames which encode the amino acid sequence (SEQ ID NO:2, SEQ ID NO:7 and SEQ ID NO:11) of human Tango-77. 15 The three potential open reading frames of SEQ ID NO:1 extend from: (1) nucleotide 356 to nucleotide 889 (SEQ ID NO:3); (2) nucleotide 389 to nucleotide 889 (SEQ ID NO:6); and (3) nucleotide 481 to nucleotide 889 (SEQ ID NO:10).

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Figure 2 depicts an alignment of an amino acid sequence of Tango-77 (T77; SEQ ID NO:2) with IL-1RA (SEQ ID NO:14), and IL-1 β (SEQ ID NO:15).

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Figure 3 depicts the genomic sequence of BAC1 (SEQ ID NO:16).

Figure 4 depicts the genomic sequence of BAC2 (SEQ ID NO:17).

Figure 5 depicts an amino acid sequence of an alternatively spliced form of Tango-77 (SEQ ID NO:2) as predicted by Procrustes (T77-procrustes; SEQ ID NO:18).

30

Figure 6 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with Tango-77 (SEQ ID NO:2).

- 10 -

Figure 7 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with IL-1 α (SEQ ID NO:14), and IL-1 β (SEQ ID NO:15).

5 Detailed Description of the Invention

The present invention is based on the discovery of a cDNA molecule encoding human Tango-77, a member of the cytokine superfamily. The cDNA molecule encoding human Tango-77 has three possible open reading frames. The 10 three possible nucleotide open reading frames for human Tango-77 protein are shown in Figure 1 (SEQ ID NO:3, SEQ ID NO:6 and SEQ ID NO:10). The predicted amino acid sequence for the three possible Tango-77 immature proteins are also shown in
15 Figure 1 (SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11) and three possible mature proteins are also shown in Figure 1 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13).

The Tango-77 cDNA of Figure 1 (SEQ ID NO:1), which is approximately 989 nucleotides long including 20 untranslated regions, encodes a protein amino acid having a molecular weight of approximately 19 kDa, 18 kDa, or 14.9 KDa (excluding post-translational modifications) and the possible mature form of the protein has a molecular weight of 13 kDa. A plasmid containing a cDNA encoding 25 human Tango-77 (with the cDNA insert name of Of fthx077) was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209 on July 2, 1998 and assigned Accession Number 98807. This deposit will be maintained under the terms 30 of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an

- 11 -

admission that a deposit is required under 35 U.S.C. §112.

Human Tango-77 is one member of a family of molecules (the "Tango-77 family") having certain 5 conserved structural and functional features. The term "family," when referring to the protein and nucleic acid molecules of the invention, is intended to mean two or more proteins or nucleic acid molecules having a common structural domain and having sufficient amino acid or 10 nucleotide sequence identity as defined herein. Such family members can be naturally occurring and can be from either the same or different species. For example, a family can contain a first protein of human origin and a homologue of that protein of murine origin, as well as a 15 second, distinct protein of human origin and a murine homologue of that protein. Members of a family may also have common functional characteristics.

As used interchangeably herein a "Tango-77 activity", "biological activity of Tango-77" or 20 "functional activity of Tango-77", refers to an activity exerted by a Tango-77 protein, polypeptide or nucleic acid molecule on a Tango-77 responsive cell as determined *in vivo*, or *in vitro*, according to standard techniques. A Tango-77 activity can be a direct activity, such as an 25 association with a second protein, or an indirect activity, such as a cellular signaling activity mediated by interaction of the Tango-77 protein with a second protein. In a preferred embodiment, a Tango-77 activity includes at least one or more of the following 30 activities: (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in

- 12 -

inflammation, and (v) the ability to bind the IL-1 receptor.

Accordingly, another embodiment of the invention features isolated Tango-77 proteins and polypeptides 5 having a Tango-77 activity.

Yet another embodiment of the invention features Tango-77 molecules which contain a signal sequence. Generally, a signal sequence (or signal peptide) is a peptide containing about 21 to 63 amino acids which 10 occurs at the extreme N-terminal end of a secretory protein. The native Tango-77 signal sequence (SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells), 15 expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence. Alternatively, the native Tango-77 signal 20 sequence can itself be used as a heterologous signal sequence in expression systems, e.g., to facilitate the secretion of a protein of interest.

Various aspects of the invention are described in further detail in the following subsections.

25 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules that encode Tango-77 proteins or biologically active portions thereof, as well as nucleic acid molecules sufficient for use as hybridization probes 30 to identify Tango-77-encoding nucleic acids (e.g., Tango-77 mRNA) and fragments for use as PCR primers for the amplification or mutation of Tango-77 nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g.,

- 13 -

cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences (preferably protein encoding sequences) which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated Tango-77 nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement of any of these nucleotide sequences, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof as a hybridization probe, Tango-77 nucleic acid molecules can be isolated using standard

- 14 -

hybridization and cloning techniques (e.g., as described in Sambrook et al., eds., *Molecular Cloning: A Laboratory Manual, 2nd ed.*, Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold

5 Spring Harbor, NY, 1989).

A nucleic acid of the invention can be amplified using cDNA, mRNA or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so
10 amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to Tango-77 nucleotide sequences can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

15 In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 the cDNA of ATCC 98807, or a
20 portion thereof. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

25 Moreover, the nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence encoding Tango-77, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of Tango-77. The nucleotide
30 sequence determined from the cloning of the human Tango-77 gene allows for the generation of probes and primers designed for use in identifying and/or cloning Tango-77 homologues in other cell types, e.g., from other tissues, as well as Tango-77 homologues from other
35 mammals. The probe/primer typically comprises

- 15 -

substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25,
5 more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.
Alternatively, the oligonucleotide can typically comprise
10 a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of a naturally occurring
15 mutant of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

Probes based on the human Tango-77 nucleotide sequence can be used to detect transcripts or genomic sequences encoding the same or identical proteins. The probe comprises a label group attached thereto, e.g., a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express a Tango-77 protein, such as by
20 measuring a level of a Tango-77-encoding nucleic acid in a sample of cells from a subject, e.g., detecting
25 Tango-77 mRNA levels or determining whether a genomic Tango-77 gene has been mutated or deleted.

A nucleic acid fragment encoding a "biologically active portion of Tango-77" can be prepared by isolating a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the nucleotide sequence of the cDNA of ATCC 98807 which encodes a polypeptide having a Tango-77 biological activity, expressing the encoded portion of
30 Tango-77 protein (e.g., by recombinant expression in
35

- 16 -

vitro) and assessing the activity of the encoded portion of Tango-77.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence of SEQ 5 ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 due to degeneracy of the genetic code and thus encode the same Tango-77 protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 10 98807.

In addition to the human Tango-77 nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807, it will be appreciated by those skilled in the art that DNA sequence 15 polymorphisms that lead to changes in the amino acid sequences of Tango-77 may exist within a population (e.g., the human population). Such genetic polymorphism in the Tango-77 gene may exist among individuals within a population due to natural allelic variation. An allele 20 is one of a group of genes which occur alternatively at a given genetic locus. As used herein, the term "allelic variant" refers to a nucleotide sequence which occurs at a Tango-77 locus or to a polypeptide encoded by the nucleotide sequence. As used herein, the terms "gene" 25 and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a Tango-77 protein, preferably a mammalian Tango-77 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the Tango-77 gene. 30 Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and 35 resulting amino acid polymorphisms or variations in

- 17 -

Tango-77 that are the result of natural allelic variation and that do not alter the functional activity of Tango-77 are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding Tango-77 5 proteins from other species (Tango-77 homologues), which have a nucleotide sequence which differs from that of a human Tango-77, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the Tango-77 10 cDNA of the invention can be isolated based on their identity to the human Tango-77 nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

15 Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, or 989) nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule 20 comprising the nucleotide sequence, preferably the coding sequence, of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions 25 for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols* 30 in *Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 35 50-65°C. Preferably, an isolated nucleic acid molecule

- 18 -

of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof, corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

In addition to naturally-occurring allelic variants of the Tango-77 sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807, thereby leading to changes in the amino acid sequence of the encoded Tango-77 protein, without altering the biological activity of the Tango-77 protein. Amino acid residues that are not conserved or only semiconserved among Tango-77 of various species may be non-essential for activity and thus would likely be targets for alteration.

Alternatively, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of Tango-77 (e.g., the sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the Tango-77 proteins of various species may be essential for activity and thus would not likely be targets for alteration, unless one wishes to reduce or alter Tango-77 activity.

Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding Tango-77

- 19 -

proteins that contain changes in amino acid residues that are not essential for activity. Such Tango-77 proteins differ in amino acid sequence from SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule includes a nucleotide sequence encoding a protein that includes an amino acid sequence that is at least about 45% identical, 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

An isolated nucleic acid molecule encoding a Tango-77 protein having a sequence which differs from that of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine,

- 20 -

valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

- 5 Thus, a predicted nonessential amino acid residue in Tango-77 is preferably replaced with another amino acid residue from the same side chain family. Alternatively, mutations can be introduced randomly along all or part of a Tango-77 coding sequence, such as by saturation
10 mutagenesis, and the resultant mutants can be screened for Tango-77 biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

15 In a preferred embodiment, a mutant Tango-77 protein can be assayed for: (1) the ability to form protein:protein interactions with proteins in the Tango-77 signalling pathway; (2) the ability to bind a Tango-77 ligand or receptor; or (3) the ability to bind
20 to an intracellular target protein or (4) the ability to interact with a protein involved in inflammation or (5) the ability to bind the IL-1 receptor. In yet another preferred embodiment, a mutant Tango-77 can be assayed for the ability to modulate inflammation, asthma,
25 autoimmune diseases, and sepsis.

The present invention encompasses antisense nucleic acid molecules, i.e., molecules which are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire Tango-77 coding strand, or to only a portion thereof, e.g., all or
35 part of the protein coding region (or open reading

- 21 -

frame). An antisense nucleic acid molecule can be antisense to a noncoding region of the coding strand of a nucleotide sequence encoding Tango-77. The noncoding regions ("5' and 3' untranslated regions") are the 5' and 5 3' sequences which flank the coding region and are not translated into amino acids.

Given the coding strand sequences encoding Tango-77 disclosed herein (e.g., SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:8), antisense nucleic acids of the invention 10 can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of Tango-77 mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or 15 noncoding region of Tango-77 mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of Tango-77 mRNA, e.g., an oligonucleotide having the sequence 5'-TGCAACTTTACAGGAAACAC-3' (SEQ ID NO:19) or 20 5'-CCTCACTTTACCCGAGACTC-3' (SEQ ID NO:20) or 5'-GACGGGTGGTACTTAAACAA-3' (SEQ ID NO:21). An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be 25 constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously 30 modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. 35 Examples of modified nucleotides which can be used to

- 22 -

generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-
5 carboxymethylaminomethyl-2-thiouridine,
5-carboxymethylaminomethyluracil, dihydrouracil,
beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-
10 methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine,
5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid
15 (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil
20 (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an
25 antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a Tango-77 protein to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, 35 in the case of an antisense nucleic acid molecule which

- 23 -

- binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein.
- To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.
- An antisense nucleic acid molecule of the invention can be an α -anomeric nucleic acid molecule. An α -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other (Gaultier et al. (1987) *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue et al. (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead

- 24 -

ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave Tango-77 mRNA transcripts to thereby inhibit translation of Tango-77 mRNA. A ribozyme having specificity for a
5 Tango-77-encoding nucleic acid can be designed based upon the nucleotide sequence of a Tango-77 cDNA disclosed herein (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10). For example, a derivative of a *Tetrahymena* L-
19 IVS RNA can be constructed in which the nucleotide
10 sequence of the active site is complementary to the nucleotide sequence to be cleaved in a Tango-77-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742.
Alternatively, Tango-77 mRNA can be used to select a
15 catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel and Szostak (1993) *Science* 261:1411-1418.

The invention also encompasses nucleic acid molecules which form triple helical structures. For
20 example, Tango-77 gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the Tango-77 (e.g., the Tango-77 promoter and/or enhancers) to form triple helical structures that prevent transcription of the Tango-77
25 gene in target cells. See generally, Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

In preferred embodiments, the nucleic acid
30 molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate
35 peptide nucleic acids (see Hyrup et al. (1996) *Bioorganic*

- 25 -

& Medicinal Chemistry 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, e.g., DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup et al. (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675.

PNAs of Tango-77 can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antogene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of Tango-77 can also be used, e.g., in the analysis of single base pair mutations in a gene by, e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S1 nucleases (Hyrup (1996) *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675).

In another embodiment, PNAs of Tango-77 can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of Tango-77 can be generated which may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, e.g., RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion

- 26 -

would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation 5 (Hyrup (1996) *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) *supra* and Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry 10 and modified nucleoside analogs. Compounds such as 5'- (4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can be used as a link between the PNA and the 5' end of DNA (Mag et al. (1989) *Nucleic Acid Res.* 17:5973-88). PNA monomers are then coupled in a stepwise manner to 15 produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser et al. (1975) *Bioorganic Med. Chem. Lett.* 20 5:1119-1124).

In other embodiments, the oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, 25 e.g., Letsinger et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. WO 88/09810) or the blood-brain barrier (see, e.g., PCT Publication No. WO 89/10134). In addition, oligonucleotides can be 30 modified with hybridization-triggered cleavage agents (see, e.g., Krol et al. (1988) *Bio/Techniques* 6:958-976) or intercalating agents (see, e.g., Zon (1988) *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide,

- 27 -

hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

II. Isolated Tango-77 Proteins and Anti-Tango-77 Antibodies

5 One aspect of the invention pertains to isolated Tango-77 proteins, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-Tango-77 antibodies. In one embodiment, native Tango-77 proteins can be isolated
10 from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, Tango-77 proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a Tango-77 protein or polypeptide
15 can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from
20 the cell or tissue source from which the Tango-77 protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of Tango-77 protein in which the
25 protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, Tango-77 protein that is substantially free of cellular material includes preparations of Tango-77 protein having less than about 30%, 20%, 10%, or
30 5% (by dry weight) of non-Tango-77 protein (also referred to herein as a "contaminating protein"). When the Tango-77 protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture

- 28 -

medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When Tango-77 protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of Tango-77 protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or non-Tango-77 chemicals.

Biologically active portions of a Tango-77 protein include peptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the Tango-77 protein (e.g., the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13), which include fewer amino acids than the full length Tango-77 proteins, and exhibit at least one activity of a Tango-77 protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the Tango-77 protein. A biologically active portion of a Tango-77 protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length.

Moreover, other biologically active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native Tango-77 protein.

Preferred Tango-77 protein has the amino acid sequence shown of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. Other useful Tango-77 proteins are substantially identical to SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retain the functional activity of the protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet differ in

- 29 -

amino acid sequence due to natural allelic variation or mutagenesis. Accordingly, a useful Tango-77 protein is a protein which includes an amino acid sequence at least about 45%, preferably 55%, 65%, 75%, 85%, 95%, or 99%
5 identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retains the functional activity of the Tango-77 proteins of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. In a
10 preferred embodiment, the Tango-77 protein retains a functional activity of the Tango-77 protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues 20 or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at
25 that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity = # of identical positions/total # of positions, e.g., overlapping x 100). Preferably, the two sequences are
30 the same length.

The determination of percent homology between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990)
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- 30 -

Proc. Natl. Acad. Sci. USA 87:2264-2268, modified as in Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul, et al. (1990)

5 J. Mol. Biol. 215:403-410. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to Tango-77 nucleic acid molecules of the invention.

BLAST protein searches can be performed with the XBLAST

10 program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to Tango-77 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (1997) Nucleic Acids Res. 25:3389-3402.

15 When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>. Another preferred, non-limiting example of a mathematical algorithm utilized for

20 the comparison of sequences is the algorithm of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a

25 PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating

30 percent identity, only exact matches are counted.

The invention also provides Tango-77 chimeric or fusion proteins. As used herein, a Tango-77 "chimeric protein" or "fusion protein" comprises a Tango-77 polypeptide operably linked to a non-Tango-77

35 polypeptide. A "Tango-77 polypeptide" refers to a

- 31 -

polypeptide having an amino acid sequence corresponding to Tango-77 polypeptides, whereas a "non-Tango-77 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not substantially identical to the Tango-77 protein, e.g., a protein which is different from the Tango-77 protein and which is derived from the same or a different organism. Within a Tango-77 fusion protein the Tango-77 polypeptide can correspond to all or a portion of a Tango-77 protein, preferably at least one biologically active portion of a Tango-77 protein. Within the fusion protein, the term "operably linked" is intended to indicate that the Tango-77 polypeptide and the non-Tango-77 polypeptide are fused in-frame to each other. The non-Tango-77 polypeptide can be fused to the N-terminus or C-terminus of the Tango-77 polypeptide.

One useful fusion protein is a GST-Tango-77 fusion protein in which the Tango-77 sequences are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant Tango-77.

In another embodiment, the fusion protein is a Tango-77 protein containing a heterologous signal sequence at its N-terminus. For example, the native Tango-77 signal sequence (i.e., about amino acids 1 to 63 of SEQ ID NO:2; SEQ ID NO:4; or about amino acids 1 to 52 of SEQ ID NO:7; SEQ ID NO:8; or about amino acids 1 to 21 of SEQ ID NO:11; SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells), expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel et al., *supra*). Other examples of eukaryotic heterologous signal sequences include the secretory sequences of

- 32 -

melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook et al., 5 supra) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an Tango-77-immunoglobulin fusion protein in which all or part of Tango-77 is fused to sequences derived from a 10 member of the immunoglobulin protein family. The Tango-77-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a Tango-77 ligand and a Tango-77 receptor on the 15 surface of a cell, to thereby suppress Tango-77-mediated signal transduction *in vivo*. The Tango-77-immunoglobulin fusion proteins can be used to affect the bioavailability of a Tango-77 cognate ligand. Inhibition of the Tango-77 ligand/Tango-77 interaction may be useful therapeutically 20 for both the treatment of inflammatory and autoimmune disorders. Moreover, the Tango-77-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-Tango-77 antibodies in a subject, to purify Tango-77 ligands and in screening assays to identify 25 molecules which inhibit the interaction of Tango-77 with a Tango-77 receptor.

Preferably, a Tango-77 chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the 30 different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as 35 appropriate, alkaline phosphatase treatment to avoid

- 33 -

undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene 5 fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., *Current Protocols in Molecular 10 Biology*, Ausubel et al. eds., John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An Tango-77-encoding nucleic acid can be cloned into such an expression vector such that the 15 fusion moiety is linked in-frame to the Tango-77 protein.

The present invention also pertains to variants of the Tango-77 proteins (i.e., proteins having a sequence which differs from that of the Tango-77 amino acid sequence). Such variants can function as either Tango-77 20 agonists (mimetics) or as Tango-77 antagonists. Variants of the Tango-77 protein can be generated by mutagenesis, e.g., discrete point mutation or truncation of the Tango-77 protein. An agonist of the Tango-77 protein can retain substantially the same, or a subset, of the 25 biological activities of the naturally occurring form of the Tango-77 protein. An antagonist of the Tango-77 protein can inhibit one or more of the activities of the naturally occurring form of the Tango-77 protein by, for example, competitively binding to a downstream or 30 upstream member of a cellular signaling cascade which includes the Tango-77 protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the 35 naturally occurring form of the protein can have fewer

- 34 -

side effects in a subject relative to treatment with the naturally occurring form of the Tango-77 proteins.

Variants of the Tango-77 protein which function as either Tango-77 agonists (mimetics) or as Tango-77 antagonists can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the Tango-77 protein for Tango-77 protein agonist or antagonist activity. In one embodiment, a variegated library of Tango-77 variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of Tango-77 variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential Tango-77 sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of Tango-77 sequences therein. There are a variety of methods which can be used to produce libraries of potential Tango-77 variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential Tango-77 sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, e.g., Narang (1983) *Tetrahedron* 39:3; Itakura et al. (1984) *Annu. Rev. Biochem.* 53:323; Itakura et al. (1984) *Science* 198:1056; Ike et al. (1983) *Nucleic Acid Res.* 11:477).

In addition, libraries of fragments of the Tango-77 protein coding sequence can be used to generate a variegated population of Tango-77 fragments for

- 35 -

screening and subsequent selection of variants of a Tango-77 protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a Tango-77 coding sequence with 5 a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed 10 duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal and internal fragments of various sizes of the Tango-77 protein.

15 Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the 20 gene libraries generated by the combinatorial mutagenesis of Tango-77 proteins. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, 25 transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble 30 mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify Tango-77 variants (Arkin and Yourvan (1992) Proc. Natl. Acad. Sci. USA 89:7811-7815; Delgrave et al. (1993) 35 Protein Engineering 6(3):327-331).

- 36 -

An isolated Tango-77 protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind Tango-77 using standard techniques for polyclonal and monoclonal antibody preparation. The 5 full-length Tango-77 protein can be used or, alternatively, the invention provides antigenic peptide fragments of Tango-77 for use as immunogens. The antigenic peptide of Tango-77 comprises at least 8 (preferably 10, 15, 20, or 30) amino acid residues of the 10 amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13 and encompasses an epitope of Tango-77 such that an antibody raised against the peptide forms a specific immune complex with Tango-77.

15 A Tango-77 immunogen typically is used to prepare antibodies by immunizing a suitable subject (e.g., rabbit, goat, mouse or other mammal) with the immunogen. An appropriate immunogenic preparation can contain, for example, recombinantly expressed Tango-77 protein or a 20 chemically synthesized Tango-77 polypeptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or similar immunostimulatory agent. Immunization of a suitable subject with an immunogenic Tango-77 preparation induces 25 a polyclonal anti-Tango-77 antibody response.

Accordingly, another aspect of the invention pertains to anti-Tango-77 antibodies. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of 30 immunoglobulin molecules, i.e., molecules that contain an antigen binding site which specifically binds an antigen, such as Tango-77. A molecule which specifically binds to Tango-77 is a molecule which binds Tango-77, but does not substantially bind other molecules in a sample, e.g., a 35 biological sample, which naturally contains Tango-77.

- 37 -

Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')₂, fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides

5 polyclonal and monoclonal antibodies that bind Tango-77. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a

10 particular epitope of Tango-77. A monoclonal antibody composition thus typically displays a single binding affinity for a particular Tango-77 protein with which it immunoreacts.

Polyclonal anti-Tango-77 antibodies can be

15 prepared as described above by immunizing a suitable subject with a Tango-77 immunogen. The anti-Tango-77 antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized

20 Tango-77. If desired, the antibody molecules directed against Tango-77 can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. At an appropriate time after

25 immunization, e.g., when the anti-Tango-77 antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein

30 (1975) *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al. (1983) *Immunol Today* 4:72), the EBV-hybridoma technique (Cole et al. (1985), *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for

35 producing hybridomas is well known (see generally Current

Protocols in Immunology (1994) Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Briefly, an immortal cell line (typically a myeloma) is fused to lymphocytes (typically splenocytes) from a mammal immunized with a 5 Tango-77 immunogen as described above, and the culture supernatants of the resulting hybridoma cells are screened to identify a hybridoma producing a monoclonal antibody that binds Tango-77.

Any of the many well known protocols used for 10 fusing lymphocytes and immortalized cell lines can be applied for the purpose of generating an anti-Tango-77 monoclonal antibody (see, e.g., Current Protocols in Immunology, *supra*; Galfre et al. (1977) *Nature* 266:55052; R.H. Kenneth, in *Monoclonal Antibodies: A New Dimension* 15 *In Biological Analyses*, Plenum Publishing Corp., New York, New York (1980); and Lerner (1981) *Yale J. Biol. Med.*, 54:387-402. Moreover, the ordinarily skilled worker will appreciate that there are many variations of such methods which also would be useful. Typically, the 20 immortal cell line (e.g., a myeloma cell line) is derived from the same mammalian species as the lymphocytes. For example, murine hybridomas can be made by fusing lymphocytes from a mouse immunized with an immunogenic preparation of the present invention with an immortalized 25 mouse cell line, e.g., a myeloma cell line that is sensitive to culture medium containing hypoxanthine, aminopterin and thymidine ("HAT medium"). Any of a number of myeloma cell lines can be used as a fusion partner according to standard techniques, e.g., the P3- 30 NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines. These myeloma lines are available from ATCC. Typically, HAT-sensitive mouse myeloma cells are fused to mouse 35 splenocytes using polyethylene glycol ("PEG"). Hybridoma cells resulting from the fusion are then selected using HAT medium, which kills unfused and unproductively fused

- 39 -

myeloma cells (unfused splenocytes die after several days because they are not transformed). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants 5 for antibodies that bind Tango-77, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal anti-Tango-77 antibody can be identified and isolated by screening a recombinant 10 combinatorial immunoglobulin library (e.g., an antibody phage display library) with Tango-77 to thereby isolate immunoglobulin library members that bind Tango-77. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant 15 *Phage Antibody System*, Catalog No. 27-9400-01; and the Stratagene *SurfZAP™ Phage Display Kit*, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, 20 U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 25 92/09690; PCT Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734.

Additionally, recombinant anti-Tango-77 30 antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be 35 produced by recombinant DNA techniques known in the art,

- 40 -

for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533;

5 U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al. (1988) *Science* 240:1041-1043; Liu et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al. (1987) *J. Immunol.* 139:3521-3526; Sun et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura 10 et al. (1987) *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al. (1988) *J. Natl. Cancer Inst.* 80:1553-1559); Morrison (1985) *Science* 229:1202-1207; Oi et al. (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al. (1986) *Nature* 15 321:552-525; Verhoeven et al. (1988) *Science* 239:1534; and Beidler et al. (1988) *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice 20 which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of Tango-77.

25 Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible 30 to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion 35 of this technology for producing human antibodies and

- 41 -

human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, 5 companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to the described above.

Completely human antibodies which recognize a 10 selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope.

15 First, a non-human monoclonal antibody which binds a selected antigen (epitope), e.g., an antibody which inhibits Tango-77 activity, is identified. The heavy chain and the light chain of the non-human antibody are cloned and used to create phage display Fab fragments. 20 For example, the heavy chain gene can be cloned into a plasmid vector so that the heavy chain can be secreted from bacteria. The light chain gene can be cloned into a phage coat protein gene so that the light chain can be expressed on the surface of phage. A repertoire (random 25 collection) of human light chains fused to phage is used to infect the bacteria which express the non-human heavy chain. The resulting progeny phage display hybrid antibodies (human light chain/non-human heavy chain). The selected antigen is used in a panning screen to 30 select phage which bind the selected antigen. Several rounds of selection may be required to identify such phage. Next, human light chain genes are isolated from the selected phage which bind the selected antigen. These selected human light chain genes are then used to 35 guide the selection of human heavy chain genes as

- 42 -

follows. The selected human light chain genes are inserted into vectors for expression by bacteria. Bacteria expressing the selected human light chains are infected with a repertoire of human heavy chains fused to 5 phage. The resulting progeny phage display human antibodies (human light chain/human heavy chain).

Next, the selected antigen is used in a panning screen to select phage which bind the selected antigen. The phage selected in this step display completely human 10 antibody which recognize the same epitope recognized by the original selected, non-human monoclonal antibody.... The genes encoding both the heavy and light chains are readily isolated and be further manipulated for production of human antibody. This technology is 15 described by Jespers et al. (1994, *Bio/technology* 12:899-903).

An anti-Tango-77 antibody (e.g., monoclonal antibody) can be used to isolate Tango-77 by standard techniques, such as affinity chromatography or 20 immunoprecipitation. An anti-Tango-77 antibody can facilitate the purification of natural Tango-77 from cells and of recombinantly produced Tango-77 expressed in host cells. Moreover, an anti-Tango-77 antibody can be used to detect Tango-77 protein (e.g., in a cellular 25 lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the Tango-77 protein. Anti-Tango-77 antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for 30 example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, 35 bioluminescent materials, and radioactive materials.

- 43 -

Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and 5 avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of 10 bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{35}S or ^3H .

III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to 15 vectors, preferably expression vectors, containing a nucleic acid molecule encoding Tango-77 (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of 20 vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous 25 replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon 30 introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant

- 44 -

DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, 5 adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a 10 host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant 15 expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an *in vitro* transcription/translation system or in a host cell 20 when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in 25 Goeddel; *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of 30 the nucleotide sequence only in certain host cells (e.g., tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level 35 of expression of protein desired, etc. The expression

- 45 -

vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (e.g., Tango-77 proteins, mutant forms 5 of Tango-77, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of Tango-77 in prokaryotic or eukaryotic cells, e.g., bacterial cells such as *E. coli*, insect cells (using baculovirus 10 expression vectors), yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and 15 translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the 20 expression of either fusion or non-fusion proteins.

Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant 25 protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction 30 of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. 35 Typical fusion expression vectors include pGEX (Pharmacia

- 46 -

Biotech Inc; Smith and Johnson (1988) *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein 5 A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann et al. (1988) *Gene* 69:301-315) and pET 11d (Studier et al., *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, 10 San Diego, California (1990) 60-89). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 gn10-lac fusion 15 promoter mediated by a coexpressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident λ prophage harboring a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter.

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, *Gene Expression Technology: Methods in Enzymology* 185, 20 Academic Press, San Diego, California (1990) 119-128). Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada et al. 25 (1992) *Nucleic Acids Res.* 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the Tango-77 expression vector is a yeast expression vector. Examples of vectors 30 for expression in yeast *S. cerevisiae* include pYEPSec1

- 47 -

(Baldari et al. (1987) *EMBO J.* 6:229-234), pMFA (Kurjan and Herskowitz (1982) *Cell* 30:933-943), pJRY88 (Schultz et al. (1987) *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and picZ (InVitrogen Corp, 5 San Diego, CA).

Alternatively, Tango-77 can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series 10 (Smith et al. (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a 15 mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed (1987) *Nature* 329:840) and pMT2PC (Kaufman et al. (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral 20 regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook et al. (*supra*).

25 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory 30 elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert et al. (1987) *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) *Adv. Immunol.* 43:235-275), in particular 35 promoters of T cell receptors (Winoto and Baltimore

- 48 -

(1989) *EMBO J.* 8:729-733) and immunoglobulins (Banerji et al. (1983) *Cell* 33:729-740; Queen and Baltimore (1983) *Cell* 33:741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle (1989) *Proc. 5 Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund et al. (1985) *Science* 230:912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-
10 regulated promoters are also encompassed, for example the murine *hox* promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the α -fetoprotein promoter (Campes and Tilghman (1989) *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA 20 molecule) of an RNA molecule which is antisense to Tango-77 mRNA. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for 25 instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in 30 which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see

- 49 -

Weintraub et al. (*Reviews - Trends in Genetics*, Vol. 1(1) 1986).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the 5 invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications 10 may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

15 A host cell can be any prokaryotic or eukaryotic cell. For example, Tango-77 protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known 20 to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer 25 to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for 30 transforming or transfecting host cells can be found in Sambrook, et al. (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of 35 cells may integrate the foreign DNA into their genome.

- 50 -

In order to identify and select these integrants, a gene that encodes a selectable marker (e.g., for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable 5 markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding Tango-77 or can be introduced on a separate vector. Cells stably 10 transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a 15 prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) Tango-77 protein. Accordingly, the invention further provides methods for producing Tango-77 protein using the host cells of the invention. In one embodiment, the method comprises 20 culturing the host cell of invention (into which a recombinant expression vector encoding Tango-77 has been introduced) in a suitable medium such that Tango-77 protein is produced. In another embodiment, the method further comprises isolating Tango-77 from the medium or 25 the host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which 30 Tango-77-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous Tango-77 sequences have been introduced into their genome or homologous recombinant animals in which endogenous Tango-77 35 sequences have been altered. Such animals are useful for

- 51 -

studying the function and/or activity of Tango-77 and for identifying and/or evaluating modulators of Tango-77 activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous Tango-77 gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing Tango-77-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The Tango-77 cDNA sequence e.g., that of (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6; SEQ ID NO:10 or the cDNA of ATCC 98807) can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of the human Tango-77 gene, such as a mouse Tango-77 gene, can be isolated based on hybridization to the human Tango-77 cDNA and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency

- 52 -

of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the Tango-77 transgene to direct expression of Tango-77 protein to particular cells. Methods for generating 5 transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the* 10 *Mouse Embryo* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the Tango-77 transgene in its genome and/or expression 15 of Tango-77 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding Tango-77 can further be bred to other transgenic animals carrying 20 other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a Tango-77 gene (e.g., a human or a non-human homolog of the Tango-77 gene, e.g., a murine Tango-77 gene) into 25 which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the Tango-77 gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous Tango-77 gene is functionally disrupted (i.e., 30 no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous Tango-77 gene is mutated or otherwise altered but still encodes functional protein (e.g., the 35 upstream regulatory region can be altered to thereby

- 53 -

alter the expression of the endogenous Tango-77 protein). In the homologous recombination vector, the altered portion of the Tango-77 gene is flanked at its 5' and 3' ends by additional nucleic acid of the Tango-77 gene to 5 allow for homologous recombination to occur between the exogenous Tango-77 gene carried by the vector and an endogenous Tango-77 gene in an embryonic stem cell. The additional flanking Tango-77 nucleic acid is of sufficient length for successful homologous recombination 10 with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi (1987) *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic 15 stem cell line (e.g., by electroporation) and cells in which the introduced Tango-77 gene has homologously recombined with the endogenous Tango-77 gene are selected (see, e.g., Li et al. (1992) *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal 20 (e.g., a mouse) to form aggregation chimeras (see, e.g., Bradley in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, ed. (IRL, Oxford, 1987) pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and 25 the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing 30 homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication Nos. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

- 54 -

In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, e.g., Lakso et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman et al. 10 (1991) *Science* 251:1351-1355. If a *cre/loxP* recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of 15 "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut et al. (1997) *Nature* 385:810-813 and PCT Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G₀ phase. The quiescent cell can 25 then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyste and then transferred to pseudopregnant female foster animal. The offspring borne 30 of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is isolated.

- 55 -

IV. Pharmaceutical Compositions

The Tango-77 nucleic acid molecules, Tango-77 proteins, and anti-Tango-77 antibodies (also referred to herein as "active compounds") of the invention can be 5 incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is 10 intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active 15 substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

20 A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, (e.g. intravenous, intradermal, subcutaneous) (e.g., oral inhalation), transdermal 25 (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene 30 glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as 35 acetates, citrates or phosphates and agents for the

- 56 -

adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable 5 syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable 10 solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be 15 fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, 20 for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethyleneglycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance 25 of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, 30 thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including

- 57 -

in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (e.g., a Tango-77 5 protein or anti-Tango-77 antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a 10 sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and 15 freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in 20 gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier 25 for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and 30 the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a 35 lubricant such as magnesium stearate or Sterotes; a

- 58 -

glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

5 For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

10 Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and 15 include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are 20 formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention 25 enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and 30 microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to 35 those skilled in the art. The materials can also be

- 59 -

obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as 5 pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or 10 parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active 15 compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the 20 particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors. 25 Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470) or by stereotactic injection (see, e.g., Chen et al. (1994) Proc. Natl. Acad. Sci. USA 91:3054-3057). The pharmaceutical preparation of the 30 gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, e.g. 35 retroviral vectors, the pharmaceutical preparation can

- 60 -

include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with
5 instructions for administration.

V. Uses and Methods of the Invention

The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: a) screening
10 assays; b) detection assays (e.g., chromosomal mapping, tissue typing, forensic biology); c) predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenomics); and d) methods of treatment (e.g., therapeutic and prophylactic). A
15 Tango-77 protein interacts with other cellular proteins and can thus be used for regulation of inflammation. The polypeptides of the invention can be used in assays to determine biological activity. For example, they could be used in a panel of proteins for high-throughput
20 screening.

The isolated nucleic acid molecules of the invention can be used to express Tango-77 protein (e.g., via a recombinant expression vector in a host cell in gene therapy applications), to detect Tango-77 mRNA
25 (e.g., in a biological sample) or a genetic lesion in a Tango-77 gene, and to modulate Tango-77 activity. In addition, the Tango-77 proteins can be used to screen drugs or compounds which modulate the Tango-77 activity or expression as well as to treat disorders characterized
30 by insufficient or excessive production of Tango-77 protein or production of Tango-77 protein forms which have decreased or aberrant activity compared to Tango-77 wild type protein. In addition, the anti-Tango-77

- 61 -

antibodies of the invention can be used to detect and isolate Tango-77 proteins and modulate Tango-77 activity.

This invention further pertains to novel agents identified by the above-described screening assays and 5 uses thereof for treatments as described herein.

A. Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, i.e., candidate or test compounds or agents 10 (e.g., peptides, peptidomimetics, small molecules or other drugs) which bind to Tango-77 proteins or have a stimulatory or inhibitory effect on, for example, Tango-77 expression or Tango-77 activity.

Examples of methods for the synthesis of molecular 15 libraries can be found in the art, for example in: DeWitt et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6909; Erb et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:11422; Zuckermann et al. (1994). *J. Med. Chem.* 37:2678; Cho et al. (1993) *Science* 261:1303; Carell et al. (1994) *Angew. 20 Chem. Int. Ed. Engl.* 33:2059; Carell et al. (1994) *Angew. Chem. Int. Ed. Engl.* 33:2061; and Gallop et al. (1994) *J. Med. Chem.* 37:1233.

Libraries of compounds may be presented in solution (e.g., Houghten (1992) *Bio/Techniques* 13:412-25 421), or on beads (Lam (1991) *Nature* 354:82-84), chips (Fodor (1993) *Nature* 364:555-556), bacteria (U.S. Patent No. 5,223,409), spores (Patent Nos. 5,571,698; 5,403,484; and 5,223,409), plasmids (Cull et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:1865-1869) or phage (Scott and Smith 30 (1990) *Science* 249:386-390; Devlin (1990) *Science* 249:404-406; Cwirla et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6378-6382; and Felici (1991) *J. Mol. Biol.* 222:301-310).

- 62 -

In another embodiment, an assay is used to determine the ability of the test compound to modulate the activity of Tango-77 or a biologically active portion thereof, for example, by determining the ability of the

5 Tango-77 protein to bind to or interact with a Tango-77 target molecule. As used herein, a "target molecule" is a molecule with which a Tango-77 protein binds or interacts in nature, for example, a molecule on the surface of a cell. A Tango-77 target molecule can be a

10 non-Tango-77 molecule or a Tango-77 protein or polypeptide of the present invention. In one embodiment, a Tango-77 target molecule is a component of a signal transduction pathway, for example, Tango-77 may bind to a IL-1 receptor or another receptor thereby blocking the

15 receptor and inhibiting future signal transduction.

Determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by one of the methods described above. In a preferred embodiment, determining the ability of the

20 Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the

25 target (e.g., intracellular Ca^{2+} , diacylglycerol, IP₃, etc.), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (e.g., a Tango-77-responsive regulatory element operably linked to a nucleic acid

30 encoding a detectable marker, e.g. luciferase), or detecting a cellular response, for example, inflammation.

In yet another embodiment, an assay of the present invention is a cell-free assay comprising contacting a Tango-77 protein or biologically active portion thereof

35 with a test compound and determining the ability of the

- 63 -

test compound to bind to the Tango-77 protein or biologically active portion thereof. Binding of the test compound to the Tango-77 protein can be determined either directly or indirectly as described above. In a 5 preferred embodiment, the assay includes contacting the Tango-77 protein or biologically active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test 10 compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the test compound to preferentially bind to Tango-77 or biologically active portion thereof as compared to the 15 known compound.

In another embodiment, an assay is a cell-free assay comprising contacting Tango-77 protein or biologically active portion thereof with a test compound and determining the ability of the test compound to 20 modulate (e.g., stimulate or inhibit) the activity of the Tango-77 protein or biologically active portion thereof. Determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished, for example, by determining the ability of the Tango-77 25 protein to bind to a Tango-77 target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished by determining the ability 30 of the Tango-77 protein to further modulate a Tango-77 target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as previously described.

In yet another embodiment, the cell-free assay 35 comprises contacting the Tango-77 protein or biologically

- 64 -

active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein,
5 wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the Tango-77 protein to preferentially bind to or modulate the activity of a Tango-77 target molecule.

10 It is possible that membrane-bound forms of Tango-77 exist. The cell-free assays of the present invention are amenable to use of both the forms Tango-77. In the case of cell-free assays comprising a membrane-bound form of Tango-77, it may be desirable to utilize a
15 solubilizing agent such that the membrane-bound form of Tango-77 is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide,
20 Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)_n, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl=N,N-
25 dimethyl-3-ammonio-1-propane sulfonate.

In more than one embodiment of the above assay methods of the present invention, it may be desirable to immobilize either Tango-77 or its target molecule to facilitate separation of complexed from uncomplexed forms
30 of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to Tango-77, or interaction of Tango-77 with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for
35 containing the reactants. Examples of such vessels

- 65 -

include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided which adds a domain that allows one or both of the proteins to be bound to a matrix. For example, glutathione-S-transferase/ Tango-77 fusion proteins or glutathione-S-transferase/target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical Co.; St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined with the test compound or the test compound and either the non-adsorbed target protein or Tango-77 protein, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or microtitre plate wells are washed to remove any unbound components and complex formation is measured either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of Tango-77 binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either Tango-77 or its target molecule can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated Tango-77 or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals; Rockford, IL), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with Tango-77 or target molecules but which do not interfere with binding of the Tango-77 protein to its target molecule can be derivatized to the wells of the plate, and unbound target or Tango-77 trapped in the wells by antibody conjugation. Methods

- 66 -

for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the Tango-77 or target molecule, as well as 5 enzyme-linked assays which rely on detecting an enzymatic activity associated with the Tango-77 or target molecule.

In another embodiment, modulators of Tango-77 expression are identified in a method in which a cell is contacted with a candidate compound and the expression of 10 Tango-77 mRNA or protein in the cell is determined. The level of expression of Tango-77 mRNA or protein in the presence of the candidate compound is compared to the level of expression of Tango-77 mRNA or protein in the absence of the candidate compound. The candidate 15 compound can then be identified as a modulator of Tango-77 expression based on this comparison. For example, when expression of Tango-77 mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence, 20 the candidate compound is identified as a stimulator of Tango-77 mRNA or protein expression. Alternatively, when expression of Tango-77 mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate 25 compound is identified as an inhibitor of Tango-77 mRNA or protein expression. The level of Tango-77 mRNA or protein expression in the cells can be determined by methods described herein for detecting Tango-77 mRNA or protein.

30 In yet another aspect of the invention, the Tango-77 proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al. (1993) Cell 72:223-232; Madura et al. (1993) J. Biol. Chem. 268:12046-12054; 35 Bartel et al. (1993) Bio/Techniques 14:920-924; Iwabuchi

- 67 -

et al. (1993) *Oncogene* 8:1693-1696; and PCT Publication No. WO 94/10300), to identify other proteins, which bind to or interact with Tango-77 ("Tango-77-binding proteins" or "Tango-77-bp") and modulate Tango-77 activity. Such 5 Tango-77-binding proteins are also likely to be involved in the propagation of signals by the Tango-77 proteins as, for example, upstream or downstream elements of the Tango-77 pathway.

The two-hybrid system is based on the modular 10 nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for Tango-77 is fused to a gene encoding the DNA binding domain of a known 15 transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If 20 the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an Tango-77-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ) 25 which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes 30 the protein which interacts with Tango-77.

This invention further pertains to novel agents identified by the above-described screening assays and uses thereof for treatments as described herein.

B. Detection Assays

Portions or fragments of the cDNA sequence identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. For example, the sequence can be used to: (i) map the respective gene on a chromosome and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. These applications are described in the subsections below.

1. Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome.

Accordingly, Tango-77 nucleic acid molecules described herein or fragments thereof, can be used to map the location of the Tango-77 gene(s) on a chromosome. The mapping of the Tango-77 sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, a Tango-77 gene can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the Tango-77 sequences. Computer analysis of Tango-77 sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the Tango-77 sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and

- 69 -

mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow (because they lack 5 a particular enzyme) but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme, will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human 10 chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. (D'Eustachio et al. (1983) *Science* 220:919-924). Somatic cell hybrids containing only fragments of human 15 chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be 20 assigned per day using a single thermal cycler. Using the Tango-77 sequences to design oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes. Other mapping strategies which can similarly be used to map a Tango-77 sequence to 25 its chromosome include *in situ* hybridization (described in Fan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6223-27), pre-screening with labeled flow-sorted chromosomes, and pre-selection by hybridization to chromosome specific cDNA libraries.

30 Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical, 35 e.g., colcemid that disrupts the mitotic spindle. The

- 70 -

chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases will suffice to get good results at a reasonable amount of time. For a review of this technique, see Verma et al. (*Human Chromosomes: A Manual of Basic Techniques* (Pergamon Press, New York, 1988)).

Reagents for chromosome mapping can be used individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. (Such data are found, for example, in V. McKusick, *Mendelian Inheritance in Man*, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, e.g., Egeland et al. (1987) *Nature* 325:783-787.

Moreover, differences in the DNA sequences between individuals affected and unaffected with a disease

- 71 -

associated with the Tango-77 gene can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the 5 particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that 10 DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

2. Tissue Typing

15 The Tango-77 sequences of the present invention can also be used to identify individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its 20 personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. This method does not suffer from the current limitations of "Dog Tags" which can be lost, 25 switched, or stolen, making positive identification difficult. The sequences of the present invention are useful as additional DNA markers for RFLP (described in U.S. Patent 5,272,057).

Furthermore, the sequences of the present 30 invention can be used to provide an alternative technique which determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the Tango-77 sequences described herein can be used to prepare two PCR primers from the 5' and 3' ends of the

- 72 -

sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique 5 individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the present invention can be used to obtain such identification sequences from individuals and from tissue. The Tango-77 sequences of 10 the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a 15 frequency of about once per each 500 bases. Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, 20 fewer sequences are necessary to differentiate individuals. The noncoding sequences of SEQ ID NO:1 can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers which each yield a noncoding amplified sequence of 100 bases. If 25 predicted coding sequences, such as those in SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

If a panel of reagents from Tango-77 sequences 30 described herein is used to generate a unique identification database for an individual, those same reagents can later be used to identify tissue from that individual. Using the unique identification database, positive identification of the individual, living or 35 dead, can be made from extremely small tissue samples.

- 73 -

3. Use of Partial Tango-77 Sequences in Forensic Biology

DNA-based identification techniques can also be used in forensic biology. Forensic biology is a scientific field employing genetic typing of biological evidence found at a crime scene as a means for positively identifying, for example, a perpetrator of a crime. To make such an identification, PCR technology can be used to amplify DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, or semen found at a crime scene. The amplified sequence can then be compared to a standard, thereby allowing identification of the origin of the biological sample.

The sequences of the present invention can be used to provide polynucleotide reagents, e.g., PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e. another DNA sequence that is unique to a particular individual). As mentioned above, actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments.

Sequences targeted to noncoding regions of SEQ ID NO:1 are particularly appropriate for this use as greater numbers of polymorphisms occur in the noncoding regions, making it easier to differentiate individuals using this technique. Examples of polynucleotide reagents include the Tango-77 sequences or portions thereof, e.g., fragments derived from the noncoding regions of SEQ ID NO:1 having a length of at least 20 or 30 bases.

The Tango-77 sequences described herein can further be used to provide polynucleotide reagents, e.g., labeled or labelable probes which can be used in, for

- 74 -

example, an *in situ* hybridization technique, to identify a specific tissue, e.g., brain tissue. This can be very useful in cases where a forensic pathologist is presented with a tissue of unknown origin. Panels of such Tango-77 probes can be used to identify tissue by species and/or by organ type.

In a similar fashion, these reagents, e.g., Tango-77 primers or probes can be used to screen tissue culture for contamination (i.e., screen for the presence 10 of a mixture of different types of cells in a culture).

C. Predictive Medicine

The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring 15 clinical trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining Tango-77 protein and/or nucleic acid expression as well as Tango-77 20 activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant Tango-77 expression or activity. The invention 25 also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with Tango-77 protein, nucleic acid expression or activity. For example, mutations in a Tango-77 gene can be assayed in a 30 biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with Tango-77 protein, nucleic acid expression or activity.

- 75 -

Another aspect of the invention provides methods for determining Tango-77 protein, nucleic acid expression or Tango-77 activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that 5 individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to 10 determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs or other compounds) on the expression or activity of Tango-77 in 15 clinical trials.

These and other agents are described in further detail in the following sections.

1. Diagnostic Assays

An exemplary method for detecting the presence or 20 absence of Tango-77 in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes Tango-77 25 protein such that the presence of Tango-77 is detected in the biological sample. A preferred agent for detecting Tango-77 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to Tango-77 mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length Tango-77 nucleic acid, such as the nucleic acid of 30 SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent

- 76 -

conditions to Tango-77 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

A preferred agent for detecting Tango-77 protein 5 is an antibody capable of binding to Tango-77 protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')₂) can be used. The term "labeled", 10 with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with 15 another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The 20 term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect Tango-77 mRNA, protein, or genomic 25 DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of Tango-77 mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of Tango-77 protein include enzyme linked immunosorbent 30 assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of Tango-77 genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of Tango-77 35 protein include introducing into a subject a labeled anti-Tango-77 antibody. For example, the antibody can be

- 77 -

labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains 5 protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means 10 from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting Tango-77 protein, mRNA, or 15 genomic DNA, such that the presence of Tango-77 protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of Tango-77 protein, mRNA or genomic DNA in the control sample with the presence of Tango-77 protein, mRNA or genomic DNA in the test sample.

20 The invention also encompasses kits for detecting the presence of Tango-77 in a biological sample (a test sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing a disorder associated with aberrant expression of Tango-77 25 (e.g., an immunological disorder). For example, the kit can comprise a labeled compound or agent capable of detecting Tango-77 protein or mRNA in a biological sample and means for determining the amount of Tango-77 in the sample (e.g., an anti-Tango-77 antibody or an 30 oligonucleotide probe which binds to DNA encoding Tango-77, e.g., SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID NO:6, or SEQ ID NO:10). Kits may also include instruction for observing that the tested subject is 35 suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77 if the

- 78 -

amount of Tango-77 protein or mRNA is above or below a normal level.

For antibody-based kits, the kit may comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to Tango-77 protein; and, optionally (2) a second, different antibody which binds to Tango-77 protein or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit may comprise, for example: (1) an oligonucleotide, e.g., a detectably labelled oligonucleotide, which hybridizes to a Tango-77 nucleic acid sequence or (2) a pair of primers useful for amplifying a Tango-77 nucleic acid molecule;

The kit may also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent.

The kit may also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit may also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for observing whether the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77.

2. Prognostic Assays

The methods described herein can furthermore be utilized as diagnostic or prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or

- 79 -

at risk of developing a disorder associated with aberrant expression or activity. Thus, the present invention provides a method in which a test sample is obtained from a subject and Tango-77 protein or nucleic acid (e.g., 5 mRNA, genomic DNA) is detected, wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. As used herein, a "test sample" refers to a 10 biological sample obtained from a subject of interest.

For example, a test sample can be a biological fluid (e.g., serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be 15 administered an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant Tango-77 expression or activity. For example, such methods can be used to 20 determine whether a subject can be effectively treated with a specific agent or class of agents (e.g., agents of a type which decrease Tango-77 activity). Thus, the present invention provides methods for determining whether a subject can be effectively treated with an 25 agent for a disorder associated with aberrant Tango-77 expression or activity in which a test sample is obtained and Tango-77 protein or nucleic acid is detected (e.g., wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject that can be administered the 30 agent to treat a disorder associated with aberrant Tango-77 expression or activity).

The methods of the invention can also be used to detect genetic lesions or mutations in a Tango-77 gene, thereby determining if a subject with the lesioned gene 35 is at risk for a disorder characterized by aberrant

- 80 -

inflammation. In preferred embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion or mutation characterized by at least one of an alteration affecting 5 the integrity of a gene encoding a Tango-77-protein, or the mis-expression of the Tango-77 gene. For example, such genetic lesions or mutations can be detected by ascertaining the existence of at least one of: 1) a deletion of one or more nucleotides from a Tango-77 gene; 10 2) an addition of one or more nucleotides to a Tango-77 gene; 3) a substitution of one or more nucleotides of a Tango-77 gene; 4) a chromosomal rearrangement of a Tango-77 gene; 5) an alteration in the level of a messenger RNA transcript of a Tango-77 gene; 6) an 15 aberrant modification of a Tango-77 gene, such as of the methylation pattern of the genomic DNA; 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of a Tango-77 gene; 8) a non-wild type level of a Tango-77-protein; 9) an allelic loss of a Tango-77 20 gene, and 10) an inappropriate post-translational modification of a Tango-77-protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions or mutations in a Tango-77 gene. A preferred biological sample is a 25 peripheral blood leukocyte sample isolated by conventional means from a subject.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (see, e.g., U.S. Patent Nos. 4,683,195 and 30 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, e.g., Landegran et al. (1988) *Science* 241:1077-1080; and Nakazawa et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:360-364), the latter of which can be particularly useful for 35 detecting point mutations in the Tango-77-gene (see,

- 81 -

e.g., Abravaya et al. (1995) *Nucleic Acids Res.* 23:675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the 5 sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a Tango-77 gene under conditions such that hybridization and amplification of the Tango-77-gene (if present) occurs, and detecting the presence or absence of an amplification 10 product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations 15 described herein.

Alternative amplification methods include: self sustained sequence replication (Guatelli et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh, et al. (1989) *Proc. Natl. 20 Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi et al. (1988) *Bio/Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection 25 schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a Tango-77 gene from a sample cell can be identified by 30 alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in 35 fragment length sizes between sample and control DNA

- 82 -

indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, e.g., U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme 5 cleavage site.

In other embodiments, genetic mutations in Tango-77 can be identified by hybridizing a sample and control nucleic acids, e.g., DNA or RNA, to high density arrays containing hundreds or thousands of 10 oligonucleotides probes (Cronin et al. (1996) *Human Mutation* 7:244-255; Kozal et al. (1996) *Nature Medicine* 2:753-759). For example, genetic mutations in Tango-77 can be identified in two-dimensional arrays containing light-generated DNA probes as described in Cronin et al. 15 *supra*. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification 20 of point mutations. This step is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel 25 probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the Tango-77 gene and detect mutations 30 by comparing the sequence of the sample Tango-77 with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert ((1977) *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger ((1977) *Proc. Natl. Acad. 35 Sci. USA* 74:5463). It is also contemplated that any of a

- 83 -

variety of automated sequencing procedures can be utilized when performing the diagnostic assays ((1995) *Bio/Techniques* 19:448), including sequencing by mass spectrometry (see, e.g., PCT Publication No. WO 94/16101; 5 Cohen et al. (1996) *Adv. Chromatogr.* 36:127-162; and Griffin et al. (1993) *Appl. Biochem. Biotechnol.* 38:147-159).

Other methods for detecting mutations in the Tango-77 gene include methods in which protection from 10 cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers et al. (1985) *Science* 230:1242). In general, the technique of "mismatch cleavage" entails providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the 15 wild-type Tango-77 sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and 20 sample strands. RNA/DNA duplexes can be treated with RNase to digest mismatched regions, and DNA/DNA hybrids can be treated with S1 nuclease to digest mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium 25 tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton et al. (1988) *Proc. Natl. 30 Acad. Sci. USA* 85:4397; Saleeba et al. (1992) *Methods Enzymol.* 217:286-295. In a preferred embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize 35 mismatched base pairs in double-stranded DNA (so called

- 84 -

"DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in Tango-77 cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the 5 thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu et al. (1994) *Carcinogenesis* 15:1657-1662). According to an exemplary embodiment, a probe based on a Tango-77 sequence, e.g., a wild-type Tango-77 sequence, is hybridized to a cDNA or other DNA product 10 from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in 15 electrophoretic mobility will be used to identify mutations in Tango-77 genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids (Orita et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:2766; see also Cotton (1993) *Mutat. Res.* 285:125-144; Hayashi (1992) *Genet Anal Tech Appl* 9:73-79). Single-stranded DNA fragments of sample and control Tango-77 nucleic acids will be denatured and allowed to renature. The secondary structure of single- 20 stranded nucleic acids varies according to sequence, and the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by 25 using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in 30

- 85 -

electrophoretic mobility (Keen et al. (1991) *Trends Genet* 7:5).

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing 5 a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers et al. (1985) *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of 10 approximately 40 bp of high-melting GC-rich DNA by PCR.

In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner (1987) *Biophys. Chem.* 265:12753).

15 Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the 20 known mutation is placed centrally and then hybridized to target DNA under conditions which permit hybridization only if a perfect match is found (Saiki et al. (1986) *Nature* 324:163); Saiki et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6230). Such allele specific oligonucleotides 25 are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification 30 technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on 35 differential hybridization) (Gibbs et al. (1989) *Nucleic*

- 86 -

Acids Res. 17:2437-2448) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent or reduce polymerase extension (Prossner (1993) Tibtech 11:238). In addition, it may be desirable to 5 introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini et al. (1992) Mol. Cell Probes 6:1). It is anticipated that in certain embodiments amplification may also be performed using Taq ligase for amplification (Barany 10 (1991) Proc. Natl. Acad. Sci USA 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of 15 amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used, 20 e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a Tango-77 gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which Tango-77 is 25 expressed may be utilized in the prognostic assays described herein.

3. Pharmacogenomics

Agents, or modulators which have a stimulatory or 30 inhibitory effect on Tango-77 activity (e.g., Tango-77 gene expression) as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (e.g., acute or chronic inflammation and asthma) 35 associated with aberrant Tango-77 activity. In

- 87 -

conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens.

Accordingly, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common inherited enzymopathy in which the main clinical complication is haemolysis after ingestion of oxidant drugs (anti-

- 88 -

malaria, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both 5 the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug 10 effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is 15 different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience 20 exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM shows no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other 25 extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of Tango-77 protein, expression 30 of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping 35 of polymorphic alleles encoding drug-metabolizing enzymes

- 89 -

to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a Tango-77 modulator, such as a modulator identified by one of the exemplary screening assays described herein.

4. Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of Tango-77 (e.g., the ability to modulate aberrant inflammation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent, as determined by a screening assay as described herein, to increase Tango-77 gene expression, increase protein levels, or upregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting decreased Tango-77 gene expression, decreased protein levels, or downregulated Tango-77 activity. Alternatively, the effectiveness of an agent, as determined by a screening assay, to decrease Tango-77 gene expression, decrease protein levels, or downregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting increased Tango-77 gene expression, increased protein levels, or upregulated Tango-77 activity.

For example, and not by way of limitation, genes, including Tango-77, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) which modulates Tango-77 activity (e.g., as identified in a screening assay described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared

- 90 -

and analyzed for the levels of expression of Tango-77 and other genes implicated in the disorder. The levels of gene expression (i.e., a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as 5 described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of Tango-77 or other genes. In this way, the gene expression pattern can serve as a marker, indicative of 10 the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In a preferred embodiment, the present invention 15 provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the 20 steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of a Tango-77 protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples 25 from the subject; (iv) detecting the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the pre-administration sample 30 with the Tango-77 protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or 35 activity of Tango-77 to higher levels than detected,

- 91 -

i.e., to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of Tango-77 to lower levels than detected, i.e., to decrease 5 the effectiveness of the agent.

C. Methods of Treatment

The present invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) developing or 10 having a disorder associated with aberrant Tango-77 expression or activity. Alternatively, disorders associated with aberrant IL-1 production can be treated with Tango-77. Such disorders include acute and chronic inflammation, asthma, some classes of arthritis, 15 autoimmune diabetes, systemic lupus erythematosus and inflammatory bowel disease.

1. Prophylactic Methods

In one aspect, the invention provides a method for preventing in a subject, a disease or condition 20 associated with an aberrant Tango-77 expression or activity (or aberrant IL-1 expression or activity), by administering to the subject an agent which modulates Tango-77 expression or at least one Tango-77 activity. Subjects at risk for a disease which is caused or 25 contributed to by aberrant Tango-77 expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms 30 characteristic of the Tango-77 aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending on the type of Tango-77 aberrancy, for example, a Tango-77 agonist or Tango-77 antagonist agent can be used for treating the

- 92 -

subject. The appropriate agent can be determined based on screening assays described herein.

2. Therapeutic Methods

Another aspect of the invention pertains to methods of modulating Tango-77 expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of Tango-77 protein activity associated with the cell. An agent that modulates Tango-77 protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of a Tango-77 protein, a peptide, a Tango-77 peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more of the biological activities of Tango-77 protein. Examples of such stimulatory agents include active Tango-77 protein and a nucleic acid molecule encoding Tango-77 that has been introduced into the cell. In another embodiment, the agent inhibits one or more of the biological activities of Tango-77 protein. Examples of such inhibitory agents include antisense Tango-77 nucleic acid molecules and anti-Tango-77 antibodies. These modulatory methods can be performed *in vitro* (e.g., by culturing the cell with the agent) or, alternatively, *in vivo* (e.g., by administering the agent to a subject). As such, the present invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of a Tango-77 protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., upregulates or downregulates) Tango-77 expression or activity. In another embodiment, the method involves

- 93 -

administering a Tango-77 protein or nucleic acid molecule as therapy to compensate for reduced or aberrant Tango-77 expression or activity.

Stimulation of Tango-77 activity is desirable in situations in which Tango-77 is abnormally downregulated and/or in which increased Tango-77 activity is likely to have a beneficial effect. Conversely, inhibition of Tango-77 activity is desirable in situations in which Tango-77 is abnormally upregulated and/or in which decreased Tango-77 activity is likely to have a beneficial effect.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patents and published patent applications cited throughout this application are hereby incorporated by reference.

EXAMPLES

Example 1: Isolation and Characterization of Human Tango-77 cDNAs

Cytokine genes IL-1 α , IL-1 β and IL-1ra have been found to be closely clustered on chromosome 2, i.e., IL-1 α , IL-1 β and IL-1ra are located within 450 kb of each other. BAC clones containing IL-1 α and IL-1 β were used to identify other proximal unknown cytokine genes. To do this, a BAC clone containing IL-1 α and IL-1 β was selected from a BAC library (Research Genetics, Huntsville, Alabama) using specific primers designed against IL-1 α and IL-1 β . The DNA from the BAC was extracted and used to make a random-sheared genomic library. From this BAC library, 4000 clones were selected for sequencing. The resulting genomic sequences were then assembled into contigs and used to screen proprietary and public data bases. One genomic contig was found to contain two

- 94 -

segments of sequences which resemble IL-1ra. These two segments are potential exons of Tango-77 gene.

Two PCR primers were then designed from the two potential exons and used to screen a panel of cDNA 5 libraries for the expression of a Tango-77 message. A cDNA library from TNF- α treated human lung epithelia showed a positive band of the predicted size (i.e., if the two exons are spliced together). Using the PCR fragment as a probe, a single cDNA clone was isolated 10 from the same library. This cDNA contains an insert of 989 bp. The cDNA clone contains three possible open reading frames. The first open reading frame encompasses 534 nucleotides (nucleotides 356-889 of SEQ ID NO:1; SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID 15 NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ 20 ID NO:5)).

The second putative nucleotide open reading frame encompasses 498 nucleotides (nucleotides 389-889 of SEQ ID NO:1; SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein includes a predicted 25 signal sequence of about 52 amino acids (from amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted mature protein of about 115 amino acids (from about amino acid 53 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

30 The third open reading frame (nucleotides 372-889 of SEQ ID NO:1; SEQ ID NO:10) encompasses 408 nucleotides and encodes a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from amino acid 1 to about amino 35 acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted

- 95 -

mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

Tango-77 is predicted to be 35% identical to human
5 IL-1ra at the amino acid level.

Example 2: Expression of Tango-77 mRNA in Human Tissues

The expression of Tango-77 was analyzed using Northern blot hybridization. A PCR generated 989 bp Tango-77 product was radioactively labeled with ^{32}P -dCTP 10 using the Prime-It kit (Stratagene; La Jolla, CA) according to the instructions of the supplier. Filters containing human mRNA (MTNI and MTNII: Clontech; Palo Alto, CA) were probed in ExpressHyb hybridization solution (Clontech) and washed at high stringency 15 according to manufacturer's recommendations.

Tango-77 mRNA was not detected in any unstimulated tissues (brain, liver, spleen, skeletal muscle, testis, pancreas, heart, kidney and peripheral blood leukocytes) mRNA on Clontech Northern blots.

20 Over 96 cDNA libraries were then tested for the presence of Tango-77 using PCR amplification. Only three libraries displayed a positive signal. These libraries were the TNF α -treated bronchoepithelium, TNF α -treated SSC cell line and anti-CD3-treated T cells.

25 Example 3: Characterization of Tango-77 Proteins

In this example, the predicted amino acid sequence of human Tango-77 protein was compared to the amino acid sequence of known protein IL-1ra. In addition, the molecular weight of the human Tango-77 proteins was 30 predicted.

The human Tango-77 cDNA (Figure 1; SEQ ID NO:1) isolated as described above encodes a 178 amino acid protein (Figure 1; SEQ ID NO:2) or a 167 amino acid

- 96 -

protein (Figure 1; SEQ ID NO:7) or a 136 amino acid protein (Figure 1; SEQ ID NO:11). The signal peptide prediction program SIGNALP Optimized Tool (Nielsen et al. (1997) *Protein Engineering* 10:1-6) predicted that

5 Tango-77 includes a 63 amino acid signal peptide (amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) preceding the 115 mature protein; or preceding the 115 mature protein (about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:8)); or preceding the 115

10 mature protein (about amino acid 21 to amino acid 136 of SEQ ID NO:11;SEQ ID NO:12).

As shown in Figure 2, Tango-77 has a region of homology to IL-1ra (SEQ ID NO:14).

Mature Tango-77 has a predicted MW of about 13 kDa and the predicted MW for the immature Tango-77 is 19.6 kDa, 18.5 kDa or 15.2 kDa, not including post-translational modifications.

Example 4: Preparation of Tango-77 Proteins

Recombinant Tango-77 can be produced in a variety of expression systems. For example, the mature Tango-77 peptide can be expressed as a recombinant glutathione-S-transferase (GST) fusion protein in *E. coli* and the fusion protein can be isolated and characterized. Specifically, as described above, Tango-77 can be fused to GST and this fusion protein can be expressed in *E. coli* strain PEB199. Expression of the GST-Tango-77 fusion protein in PEB199 can be induced with IPTG. The recombinant fusion protein can be purified from crude bacterial lysates of the induced PEB199 strain by affinity chromatography on glutathione beads.

- 97 -

Example 5: Alternatively spliced forms of IL-1ra and Tango-77

Computer program Procrustes (Gelfand et al., 1996, Proc. Natl. Acad. Sci. USA, 93:9061-9066) is an alignment algorithm that predicts the presence of alternatively spliced exons for a protein of interest in a stretch of genomic DNA. Using the IL-1ra sequence, Procrustes was used to search for the presence of additional sequences that might encode for alternatively spliced forms of IL-1ra in the two overlapping BAC genomic sequences (see Fig. 3 and Fig. 4). Potential sequences that encode variant exons for IL-1ra were identified. These predicted exons aligned well with the N-terminal region of IL-1ra, but were not present in Tango-77. The results from Procrustes predicts the existence of more spliced forms of IL-1ra.

Furthermore, Procrustes also predicted an additional sequence in BAC1 and BAC2 that encodes an alternatively spliced exon for Tango-77 (T77-procrustes; Fig. 5). This predicted splice variant form of Tango-77, T77-procrustes, was aligned with Tango-77 (Fig. 6) and with IL-1ra and IL-1 β (Fig. 7).

PCR primers within this sequence can be used to generate a product that can be used to screen a panel of cDNA libraries using standard techniques. Suitable cDNA libraries include libraries made from TNF α -treated bronchoepithelium, TNF α -treated SSC cell line and anti-CD3-treated T cells. The resulting cDNA clone(s) can be isolated from the library and sequenced to identify additional Tango-77 cDNAs.

- 98 -

Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific 5 embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

- 99 -

What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:
 - a) a nucleic acid molecule comprising a nucleotide sequence which is at least 45% identical to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
 - 10 b) a nucleic acid molecule comprising a fragment of at least 300 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
 - 15 c) nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807;
 - d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807; and
 - 30 e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,

- 100 -

SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid 5 molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:

10 a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 or the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof; and

15 b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the 20 plasmid deposited with ATCC as Accession Number 98807.

3. The nucleic acid molecule of claim 1 further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous 25 polypeptide.

5. A host cell containing the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

- 101 -

7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

5 a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID
10 NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13.

b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,
15 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule
20 comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the complement thereof under stringent conditions;

c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is
25 at least 55% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10.

9. The isolated polypeptide of claim 8 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807.

- 102 -

10. The polypeptide of claim 8 further comprising heterologous amino acid sequences.

11. An antibody which selectively binds to a polypeptide of claim 8.

5 12. A method for producing a polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID

10 NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807;

b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID

15 NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the fragment comprises at least 15 contiguous amino acids

20 of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807; and

25 c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the

30 plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid sequence of

- 103 -

SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 under stringent conditions;

comprising culturing the host cell of claim 5 under conditions in which the nucleic acid molecule is
5 expressed.

13. A method for detecting the presence of a polypeptide of claim 8 in a sample, comprising:

- a) contacting the sample with a compound which selectively binds to a polypeptide of claim 8; and
- 10 b) determining whether the compound binds to the polypeptide in the sample.

14. The method of claim 13, wherein the compound which binds to the polypeptide is an antibody.

15. A kit comprising a compound which selectively binds to a polypeptide of claim 8 and instructions for use.

16. A method for detecting the presence of a nucleic acid molecule of claim 1 in a sample, comprising the steps of:

- 20 a) contacting the sample with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule; and
- b) determining whether the nucleic acid probe or primer binds to a nucleic acid molecule in the sample.

25 17. The method of claim 16, wherein the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

- 104 -

18. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which binds to a polypeptide of claim 8 comprising the steps of:

- a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and
- 10 b) determining whether the polypeptide binds to the test compound.

20. The method of claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- 15 a) detection of binding by direct detecting of test compound/polypeptide binding;
 - b) detection of binding using a competition binding assay; and
 - c) detection of binding using an assay for
- 20 Tango-77-mediated signal transduction.s

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds to the polypeptide in a sufficient concentration to modulate the activity of the polypeptide.

- 105 -

22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

- a) contacting a polypeptide of claim 8 with a test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

GTCGACCCACGGTCCGCAGACGTACCTGGGGTCCCCTCGCGCTCCGGATGGAAAACGCCAGGGAAACTTA	79
GGCAGGCGAGCGGACGGCACCTCCCGGGACGAACACTCGGTGGCCTCTACTTCCCCGGCGTGTCCAACGCC	158
TGAGAATAACGGGACAGCGGTCGTACTCACCGACAGCGGAGCGGGCTCTCAATTGGCAAAGCACTCCAGAC	237
CTTTTGGAAGAGTGACACCAAAGGCAAGCACCTGCTGGCAGGCCCCCTAGCTCTACGCAAGTATAAGTCTGGACTT	316
M S F V G E N S G V 10	
CATTCGATTTCTGTTGAGTAATAAACTCAACGTTGAAA ATG TCC TTT GTG GGG GAG AAC TCA GGA GTG 385	
X M G S E D W E K D E P Q C C L E D P A 30	
AAA ATG GGC TCT GAG GAC TGG GAA AAA GAT GAA CCC CAG TGC TGC TTA GAA GAC CCG GCT 445	
G S P L E P G P S L P T M N F V H T K I 50	
GGA AGC CCC CTG GAA CCA CGC CCA AGC CTC CCC ACC ATG AAT TTT GTT CAC ACA AAG ATC 505	
F F A L A S S L S S A S A E K G S P I L 70	
TTC TTT GCA TTA GCC TCA TCC TTG AGC TCA GCC TCT GCG GAG AAA GGA AGT CCG ATT CTC 565	
I G V S K G E F C L Y C D K D K G Q S H 90	
CTG GGG GTC TCT AAA GGG GAG TTT TGT CTC TAC TGT GAC AAG GAT AAA GGA CAA AGT CAT 625	
P S L Q L K K E X L M K L A A Q K E S A 110	
CCA TCC CCT CAG CTG AAG AAG GAG AAA CTG ATG AAG CTG GCT GCC CAA AAG GAA TCA GCA 685	
R R P F I F Y R A Q V G S W N M L E S A 130	
CGC CGG CCC TTC ATC TTT TAT AGG GCT CAG GTG GGC TCC TGG AAC ATG CTG GAG TCG GCG 745	
A H P G W F I C T S C N C N E P V G V T 150	
GCT CAC CCC GGA TGG TTC ATC TGC ACC TCC TGC AAT TGT AAT GAG CCT GTT GGG GTG ACA 805	
D K F E N R K H I E F S F Q P V C K A E 170	
GAT AAA TTT GAG AAC AGG AAA CAC ATT GAA TTT TCA TTT CAA CCA GTT TGC AAA GCT GAA 865	
M S P S E V S D * 179	
ATG AGC CCC AGT GAG GTC AGC GAT TAG 892	
GAAACTGCCCATGAAACGCCCTCGCTAATTGAACTAATTGTATAAAAACACCAACCTGCTCACTAAAAAAA 971	
AAAAAAAAAGGGCGGCCGC 989	

Fig. 1

1/18

1	IL1ra-human T77-human IL1b-human Consensus	MEICRGLRSH LITLLFLFH SETICRPSGR KSSKMQAFRI WDVNQKTFYL ~~~~~ ~~~~~ ~~~~~ ~~~~~	50
51	IL1ra-human T77-human IL1b-human Consensus	RNNQLVAGYL QGPNVNLEEK IDVVPIEPH. ALFLGIHGGK MCISCVKSGD ~~~-MNFVHT KIFFALASSL SSASAEGKS. PILLGVSKGE FCLYCDKDKG KALHLQQDM EQQVFMSMF VQGEESNDKI PVALGLKEKN LYLSCVLKDD ~~~~~ ~~~~~ ~~~~~	100
101	IL1ra-human T77-human IL1b-human Consensus	ETR . LQLEA VNITDLSENR KODKR . FAFI RSDSGPTTSF EAAACPGWFL QSHPSLQLKK EKLMIKLAQK ESARRPFIFY RAQVGSWNML EAAAHPEWF K..PTLQLES VDPKNYP ..K KRMKMKRFVFN KIEINNKLEF EAAQFPNWY ~~~~~ ~~~~~ ~~~~~	150
151	IL1ra-human T77-human IL1b-human Consensus	CTAMEADQPV SLTNMPDEGV MVTKFYFQED E~~~~~ CTSCNCNEPV GVTDFKENRK HI .EFSFQPV CKAEMSPSEV SD STSQAENMPV FLGGT .KGQQ DITDFTEQFV SS~~~~~ -T-----PV -----F -Q-----	192

FIG. 2

2/18

>Contig1

GAAGTGAAGATAATGTATAGTAGTAATATATAATGTTAGGTGAATTAA
 AGGAAATAGAATATATTGGGGAGTAATTATGGGTGTAAGAAATATAGTA
 GGGAAAGTATTTAGATTTGAGAAAAAAAAGGAATTAGTAGTGAGGTGAA
 NAATAAAAAGNANAAGGTAAAAATTAAAAAAATTAAATATAAATAAAT
 AAATAAAAAATAAAATAAAATAAAAATTAAAAATTAAAAATATAAA
 AAAATAAAGAAATCGAAGTGGATTCTTAGAAAAAAAGAAAGTAAGGTGA
 TAGGAGGAGATAGAGAGGATGTGGTGTGAGATGATTGGTTAATTAGAAA
 ATAGGTTTGAATAGAGTGGGAAAGTAGAGTTGGTAAATGTGGGGGA
 AGAGGGTAATGTTGTTGAGTGAAGAAAAATGGTATTTTATAAAA
 TAATGAGGAAAGTGTGTGAAAAAAATTATTGGGATTGGAAAGGTGAT
 ATATAAAGTTGGAAAATTGGGGGTGGGGTTATTAGGATAAAAA
 GTTATTAAAGAATGAAAATGAATTGGTTGTAATTGGGATAAGAA
 ATTAATGTTAGAAAGAAAGGGAAAAATTGAAGAAAAAATTAGATT
 TGGAAATTAAAAATTGTGGGTAAATAGGAAGGATTTAAAGGTA
 ATTGTGGAAGGGATTGTGTGGAAAATAATAGGGAGAAAAATGGG

>Contig2

GCATCTAACTGGAGCCTGCATTATTACAGATTTAGCATCACCAAAGTCTA
 ACAATTAGACTGACTAAGGCAGAACTGCCCTTATGACAGCAGACATAAG
 AAGGAAAAGGCCAAAACACTGTGTAAAAATTATCCAAATGTGAGGAAAA
 GGCAAAAGAGAGTAGGTGTGCCCTTTAGTGTCTAACGCTGCCAAGG
 GGCATCTGATGCTCTCAGGCAGGAGTCCACAAATTTTTTGTAAGA
 TCAGATAGTAAATCTTCAGCGTAAGAGCATGAGGTCTGTCAACAAA
 TACTCAACCACCATACAACATGAAAGCAGCCAACAGACAACATGACA
 AATGAGTGTGGCTGTGTTCAAGTAAATCTGATTACAACACAGGCAAGA
 GCCCAGAGCTGACCCATGGGCCATAGTTGCTGACCCCTCTGTAAAGGA
 AAGTATTTTGTGACTGCTGTTACCATGATTGAACACAAGGCTCT
 GTAAAGTTACTGTTAACCTGCAGAAGATTGATGAGTGGCAAGTAATT
 TATTCAACAGAATAAAAATTATTCTGTTCAAGTAAAGATAAACCAA
 CTGTGATATTATGGTCCTG

>Contig3

GGGGTGTCTGCTACCATGTGCTCGAGTTCTGTAATAAAATGTTCTCTCA
 AGATCCTTAAATCTCTGGAAATTATAAAATATTGAAAGAGAAC
 AGTTTTAAATATATATATATATATATTGAGATGGAGTCTT
 GCTCTGTCGTCAGGCTGGAGTGCAGTGGCGCAAACCTGGTTACCCACAA
 CCTCTGCCCTCCGGGTTCAAGCGATTCTCTGCTCAGCCTGAGTAG
 CTGGGACTACAGGCGCCACACGCCAGCTAATTGTTGTTA
 GTAGAGACGAGGTTTACTATGTTGGCTAGGCTGGCTCAAACCTCTGAC
 CTTGTGATCTGCCGCCTGGCTCCAAAGTGTGGATTACAGGTGTG
 AGCCACTGCACCTGGCCAGTTTAAATATATTAAAACACTTGAA
 TAAGAGTCAGTGTAAACTAGAAGTTAAAATGCTTACAGAACACCCAG
 GGTTTACATTACAAGATTCTACAACAAACCTATTGAAAGGTGAGTAAG
 GCATGTTATTACAGAGAAAAGTTGGGAGCAAACACTGTAAAAATTAT
 TTTGTTGTATTCTAACAGAAAGAGTATTGTTATGTTCTAACCTC
 TGTTGATTACTACTAACGTGATTCTTGAGAGCACATGATGATGCC

>Contig4

GCCGTTCATAGAAAATGAAAGCAATAAGATGACTAGGTAAGCATGACAT
 TTAAAAGGTATTGATGGGACGTGGTTACAAAACCAACTCACAACTAAAAA
 GTCTTAGGACCTCTGCTGACTTAGGAGCCTGATCCCACACTGAGAATG
 ACTCAGTGTGTTACCTGTGGCTAGTGTAGACCAATGATCTGTCTCAGA
 GTCACTAGCCAACAGCCCATATCAAGTACTTGAAACCTTGACTCAGAAC
 CTCAGTGTCAAAACCTTGACCTAGGAACCACTGAGTGGTTAATGCA
 ATTTGCAACCCCTAGTTCAACACCGGGGGGGGGAGGGGA
 AAGGCATANANCTGATGACCTAAAGGAAACCCATTGCAAGCAACGCTT
 TGTTAAGTGTACAATTGAAATGTGTTAGAATCTCAGGTAAATGCCTT
 TGTTATTAAATGTGTGAGACAATTCTGCACATTAAAGAATATAAAAATA
 TTACCTGTAATTCCAATTGAAATGTGAAATTGACATTAGACTCTATT
 TGAATTGAAATGTCTAAAACAATGTGGTTAAGTTGAAAGGTGTG
 AATTGAGTGTGATTACTACATTAAATTCTTTTAAATTCTTTTTGG
 AGTTTAGGGATTGCTTAGATGGCTAGAAAGATTATTGATCAGATT

FIG. 3 (1 of 52)

TAAGTCTGCCTGGCAGGCACGGCAGATTTGAAAGAATCAGATATATC
 AAATTGTAGTTAAAATATTTAAGGGAACCTCAATTAACATATGCTAGAAA
 AGAGAATTAAGTATTTAGGAGGATTTAATATGGTGTGAAAGTTGTGAAAA
 TCAAAATGGAGACACTAATGTTAACAAAACCTGATAAAATGGAACCAGGG
 AAAGGCATGAAGATAGAGTTCTCACACTTGATCCCTGATCATGAAAAAG
 ATCTGC

>Contig5

GGGTTTTCCCGCTTTTACCCGAAATCTCAAGGGATGGGAAAAAGAAA
 ATTGCTAAAAATCTCGTTTTGGTTAACAGATATTTACACCNNTGG
 ATCCCATTATATGTTGCCCCAAGGTTTCGGTGGGTTCCAATCAGT
 TAGCCCCCTCCACAGTAAAGCATTACTTATCACCTCACCTAAAG
 CATAAAATCCAGCTTGAAGCTGCTCTGTTAACTGAATATATCCAC
 ATCCAAAAGTAAATGATCCATGCTCATAATCTGCCACGGATGGATGGAT
 GGATGGATGGATGGATGGATGGATGAATGGATGGATTGATTCTTG
 GAGGATTGTTGAATTGGAAATTCCACGCCAGGACAGCTGGCCCAAAC
 TGCCCGACAAATCTGCTCGGTACAAGGGAGGGTCTGGAGAGGGTGCG
 GCCCGAGCCCCAGTTGAAATGCCAACCTGGCTCTGCAGCCGGGCTTA
 GCCACTGGGTCTGGCTCCCTCATTATTAGGCCATGCCGGCTGGGG
 TGCTGCCAAGTCCCTGAGAGCACAAGCC

>Contig6

CGCGCTCAAGAAAAGCTGAAGTGTGAATGTTCTGTCTACCTTACAGTAA
 ATGCTAAGAGAATGACCAAGAGCAGAGGGTATCACTCTGCTACGGAGGA
 TTGATTGTAACTGGCTCTCCTGCCCTAGCAAGAAATGCCAGAACCATGGT
 CATTCAAGTTCTGACCAAAACTGCCCTCATGAGAACATCAACTCCCCAA
 GAAAAAAAAGCAGAAACAGGCCAAAGCTTCAGCATGGTAGGTAAACTG
 ACCCTTCTCCCTCCTTGGAGATTACACAGTAATAATGCATAAAA
 GCTTGCCAATGGACTAAGCACTGCCAGGGGTTTGTGATGCCCTGGAC
 TGAAATGCTTTTGCGTTATCATAGAATCCCAGTGCAGTCTGAGTAGA
 CTCTAAGCAAAGGGACATTTCAAAAAGCTTAAATTGCTAGTACAA
 AGAAGGCAACAAAATTCGTAACTGTGGACAGATTAACACTCACTGGTGT
 TTTGGCTTCACTGGCTTGCGAAGTACTCCTGAAGCTTCTC
 TGCGCTTCTGCAAGCAGGCCAAAGCACTGAACCTTATT
 CGAGAT

>Contig7

GAAGAGCCGCTAACCTGCTGTAGTGATAAGGAATGAACATAAGGCTAGGG
 CATATTAACATCCGCTGGTGGTGAECTTTAGCCTAGATCTTACCCCAC
 CCTGCTCCTTCCATATGGTCGGTCACTACCGATCAATGGCG
 TACTAAAAGCACTAACTATAGACTCCAACACGTCTGCGTGTGTTTACCG
 ACAAGCCGTGGAGTTAACCTCTGACAGTAGCTCAGATAAGGATGGGCT
 ATCATGGGCCCGAACCTGGGCATGACGCTCGTACCAACGCATGAGCTC
 CCCAAGTATGCTATACCTGTCCTATGAAGGGCTCAACTCTATGTGCA
 GTCCCCATGTGGAGAGTCAGGTATTGATTGATCAAGCCAGGGGTGTGGTG
 AATGGGGAGCTTCACTGGGTTAATGATAATTGAAATGCACGGTGATGG
 GGATTTCATATTGGTCTCTAAGGAGATAACAGATTGGATGCCGGGTG
 ATATTCCACTGCCAGGGTGTACCGAGGGTATCTGCAGGTGGATCTCC
 TCCCCACGTTGATTAATACCTCTGCTTGGGAAGCATAGACGGCGGGGG
 GAAATGATGAAGGGTGACCACTCCCC

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GGGAACGCAGTGTCTGTACGATGGCCTTGATTGCGAATTCTGCAGGGG
 GGG

>Contig9

GGCAAGAGATTTAATATTCCATCTCATTGGAAGATGAAAAATTG
 GGGACAGAGAGGGGAGGGGACTGGGCCAAGTTTCAAAGAAAAGTCAGT
 AGGAATTGTAATTCTGGGGGCCGGGGCCATTAGTGTGTTGGATC
 AGTAAATGGAGATGTGAGTTCAACAGTAACAGGGACATTAAATTAA
 AATGATTAAACCTTAACTGAAATGTCCTATTGTAATAATGATGGATTCA
 CAGGAAGGTACAAGAAATGTCCAGAGAGGTTGAGCCCCCTCAGCCA
 GCTTCTCCAATGTTAACATCTGCTTATTATAGTACAACATCAAAACT
 GGGAAATGATATTGGTACTGTCCAGATAGCTTACAGATTGCGCAGT
 TATACTCCACTCATTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTG

FIG. 3 (2 of 52)

4/118

TGTGTGTAGCTATG...ATTTATG1..GTAGCTTCACTGAACCCAC...
 AATCACAATACTTAACATGCCTCATCACAAAGACTCTCTTGCTATGC
 TTTACAGCTGTATCCCTTCATCTCCAAACCTAACGCCACCTCACCGCC
 TCCACCATCTCTAATCCCTGGCAACCACATTCTGTGCTCCATCTGTGTA
 ATTAATTGTGTTAATTAATGTTACAAATGGAATCATGAAGTATGTGTC
 CTTTGAGATTGGGCTGTTAATTTCACTCAGCACAATTCCGTGAGTCT
 AATCCAACCTGTGTTAGCAGTAATTCTTCCTTATTATTGCTGAATAAT
 ATGCCATGGTATGGATGTATCACAGTGTGCTAATCCTTGCCCATTGAA
 AGGAATTGGATAATTTCCAGGTTGGCTATTATGAATAAAGTGAACAT
 AAGACATGTGTGACAAATTGGTGTGATCAAAGTCTCATTCTCTGG
 GATAAAATGCCCGTAATGAAATGGCTGGGTTGTGTTGGG

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GCAAGAACACAGGCGCGTATTATAACCTACTACCAAGACCTGAACCCAT
 ATAAAGGTTATGCGTAACAATCATCATTCCCGTTCAGAAGATTACACG
 TACGACCACGCCCTGGCTACCGACTCACGTGGGCCAGTACCAAGAAATTCT
 CCCAAACAAACAGTCGTGCTGAAAACAATCGCGGTGACCTQCACGGTTA
 GAAAAGCCTGTTCAAGTCCTGGATTGCCACATATTAGCTGGGTAACT
 TTGGGCATCACATTACTCTCCGAATTTCAGATTGCAAAACTCATTG
 GATTGTTTGTGGATTGAAAGAAATAATGTAATTAGGCCGAGTGCTTT
 GACTTACGCCCTGTAATCCTATCACTTTGGGAGGCCAAGCAGGAGGGTCA
 CTTGAGCTCAGGAATTGAGACCACTCTGGCAACATAGTAGTGGAGATCCTGT
 CTCTACAAAAAAATTTTTAAATTATCCAGCATGGGGTACACGCCCTGT
 ATTCCCAGCTACTCAGGAGACTGAGGTGTGAGGATTGCTAGAACCTGGGA
 GATCAAGTCAACAGTGAGCCGTGGTGTGCCACTGCCCTCCAACCTCAGT
 GACAGAGGAAGACCCCTGCTCAAAAAAAAAAAAGTAGTAAAGTTAA
 AGAACTTAGTGTAGGCCTGGCATATAATGATATTGTTGATGTTGATGTT
 AGCTTGAGGCACATTATAGGAGTAGGGATTATAACATTATGAGCCT
 GAGAGCACATATAATGTTCCC

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GGTCTAACATGCTCCAACGTAAAGAAACCCACACTTGTCCGGCAAGGAA
 CTACTACAGATTCCTGACCTACTGTGCAATTGGGGCATGCGACGGGAC
 TGTGTTCTGGGTACGCTGTCTCAGGTTCTGGATGTAAGAATTCAA
 CTTCAGTAGTTCTCATAGACGCCGACGAGAGGGCGTCTTTCTCT
 GATGAATCTGCCAGATCTTCACTTCATAGAGTCTAAACGTCGGTGACAGCT
 ATCTACTGGAGACCCCCACGTTACAAAACGTCTAACGTCGGTGACAGCT
 CCCCACATAGGGAAAGATCACCTGAGTCTCACTACCTCACATTAGTGT
 TCTCAGCCCCATGCTATCTACGAGATGGTACCGCAGGTTAAGGGTC
 TCCGATTCCGGTGGTCCGATTCACTGTAATCGTGGCCCTACGTGAACGATC
 ACTCTGCTCGTAACATCGATACAGGGTCGGCTGACAAATGGTACTACG
 TAGGTTCTCAGGTCAATGCCCGTACGAATGAGCCTAACCTACCCATAA
 GTGCACTGTGTTACCTTCTGTTGCCAAACCTGCTACTGTATG
 CTGTGCTTGT

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AGGCTCCATGTGCTCTAGCCTGATTATCTTCAAGTGTGTTATTGCTA
 ATCTATAAGGCCCTTCTGAAATGTCACCTCATTTCTAATTAGATAT
 TTTTTTAATGTTGAGGTTCTGAGAGTCTTAGATATTAGATAACAAGT
 CCATTGTCAAATATGTGATTACAAATATTCTCTCAATCTGTAAATT
 GTTTCTCCTCTTAACAGGGCTTTGGAGAGCAGAAATTGATTTC
 ATAAGGTTCAAATTATTAAATTCTGTATAGTTACACTCTAGTGT
 TAAGTCTAAAACGTGCTCTGTCTAGGTACCAAGGTTCTCCAGTT
 TTTTTCTAGAAGTTAGAGTTCTAGTTACATTGGAGTCCATGATCC
 ATTGTTAATTAAATTCTGTATAGGTAGATGTTAGGTTAGGGTTTT
 TTAAAAAAATTACATATGTTAATTGCTCCAGTCCCTTCTGATTGAAA
 AGGGTATCCTCCCTGAAATTGCTTGTCAAGAAATTGAGACAT
 ATTGTTGAGTCTATTCTGGCTCTTACATGTTACTTTAAAAAAT
 GCATCAGTCCCTCCACCAATACCTCATTGCTTGTGATTATTGCA
 AGTTAGTAAAGCATTAGGAAAAGTGTGTTCTGCTTATTCTTNTCA
 AAAAATTGGATATTCTAGGGCTTTACATATAAAATTAAAATAACT
 TTGCTATGCTAACGAAAGCCTTATGAAGATTGATAAGAATTGCA
 TATGCCCTACATTAATTAAAAGAACTGATGTTATTGAGTT

FIG. 3 (3 of 52)

CTGCTAATCTATGAACA1..GCATCTC..CAAAGCATTAGTCTTCCTT.
 AATTTCTGTCACTTAATTTAAAATTTCACTCTAAAGATTCTGTATAT
 GTTTGTTGAATTATGCTTAAGCATTCACCTTCTTGTAAACATTATA
 AATGATTTGTGTTTATCCACTAGTCATTTCAAGTGTAGAAAA
 GCAATGAATTTGTGTTGATCTTGTCTACATCTGCAACATTAT
 TGAACTCATTTATTAGTTCTAGGAGGTTTTCACTTCTTGTAGATAC
 CTTGAGATTTCTATATAGACAGTCATGTTGTCTGCAAACAGGCACAGTT
 TTATTCTCTTCAATCTATATGCCTTTTTTTTGCTTAT
 TGCACTGGCTAGAACCTCTAGCACTATGTCAAATAGCATTGGTCAAAGCA
 GACATCCTGTTCTGTCTAGAGAACATTGGTCTTAATCTGGAT
 TGCG

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GCGCCCTTTCTCTTCAAAATTCTCTTGTCTAGTTATTGTCCAGG
 GAAATTGAAAGCTCACTTACTGTCAAGTCAGCAGGAAACAACGGTC
 TGTGCACAGCACCTAGCAAAGTTCTGCTCTAGGAATTACACTTTGGCCCT
 GAGGTAGATTCTACAAGAACCTTACCTCTAAGCAGCACTGGGTTCAT
 CTTTCCCAGTCCTCAGAGCCCATTCTACTCCTGAGTTCTCCCCACA
 AAGGACATTTCAACGTTGAGTTATTACTCAACAGAAAATGGAATGAAG
 TCCAAGACCTAAGGAGATAGAAAGGGGACCAAGTTATGGCATCTTCACC
 CCAGGACACCTGCTGATGTCCTAGTGTGAAACAGACCACTGCCCTG
 -CTCTGTAGTTGAAATGTCGCTGCAACCAGAAAGGCACCAAGGGCCAG
 ACCATGCTCTCTGTCTATCACGCCCTCAAAGCAGAATTCCAAACCTT
 GAGTCACAGTGTAAACACACGGGTGCCATAACATTGGTAAATTG
 CATTACAAAATAAAATAAAAGTTAAAATGCAATTGCTCTATTCTT
 GGGCTGGCACACTATTGCCCTGGCAAATTCCGGCCCTGACTGTTT
 TAAATAAAAGTTTATTGAAACACAACCATTGCTCTTGTACATATTGTC
 TCTGGCTGCTCGAACGCTACAATA

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GTGTTCGCTTTAAACACTTACCTAAAATTACTCTGTAATCCATGGATCC
 TTAATTATTAAAGGAACTAATGTTAATGAGTAGCTTATTTCCTCCCA
 TCTAATTAAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCCA
 CTTACATGCTTTAATGTCATATATGTTAATACCGTATACTTTAAA
 ACTTTCTAAAATAGCATTATTATAGCATGAGTGTCTATTACATTGGCA
 TATATTAGAATTTCCTTGTCTCGTTCTCTCTATTATGACTCC
 CCTCTGGATCATTTCTCTACTTGAAGTACATAGTTAGAACTGCAC
 TATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTAA
 AGTAAAATTGAGTAATATTAAAACCTAGTCTCTCATCTACTAGCCAC
 ATTTCAAGTGTCAAGCAGCCACGTGCGACTAATGACTACTGTACATCAA
 CATATAGAACATTCCATCATGGCAAAGAGCTCTATTGATAGTGTCTAC
 CAGAGTTCTGTCAGGACCAAACCTGAGGGTTGGGCTGCTATTCTCAT
 GGCCAAATAACAGATGAGATGAGCTGGGGAGGAAGAGAGTTTTATT
 CTGCNACCATTACGGGAGAAGGGCTGGAAATCATCACCAGGCCACTC
 AAAATTATTACGTTTCCAGAGCTTATACCTTCAAGCTATATGCTA
 CGTGTAAAGTGTGATTCACTGAAGACGTTAGTGTATTAACTTCTTAA
 CTGTAACTAAGGTCTGAGTCCGGAGAATCTTCCCTGGAGCCTCAGTAA
 TTTACTTAATCTAAATGGGTCAGGTGCTGGGTAATTACCTTATCTG
 TCCCCCTGCTAAATCATGGAGGTTGGGATTCTCTGACCCACAATAAA
 CTTGTTGTGGAGGCTGGGGTTCTCTGACCCACAATAAAACTGTT
 TAATCTAAATGGGCTGTTAAGAATTCTCTTATTGGTCAATT
 TAAGGCCAGAAAAGGCTGGCAAACCTTGTGATGGGCTTTGTTACAT
 TCCAGCCTTGTATAAGAACACTGGTTTAATATTAACTTAACCATT
 AGTCAGTACTGAAACAGTTGTTAGAGATCTGCAATTAGTGTGAGACCTGGC
 CTGCCACATTCTTCTGAAAGATCTTATGGTAGTGTGATCACCTTGTGA
 AAGGAAAATAATCTTGGGACCTCAAACACTAAGCAGGAAAGAAAAAGT
 CAAGCTGGGAGAATCTGACACTTAAATCCAACACTGCTAACTCATT
 CTCACTCATTCAATTATTCTTCTTCTTCTTCTTCTTCTTCTTCTT
 TTTTTGAAACGAAGTCTGCTGTCAACCAAGCTGGAGTGCAGTGGAT
 CTCAGGTCACTGCAACCTCCACCTCCGGGTCAAGCGATTCTCCTACCT
 CAGACTCCTGAGTAGCTGGATTACAGGCACCTGCCACACGCCCTGGCTA
 ATTATTATATTAGTAGAGACGGGGTTCAACATGTTCATCAGGCTGG

FIG. 3 (4 of 52)

6/118

TCTCGAACTCCTGACCTCGTATCCGC..CCCCCTGGCCTTGTGCTTGT
 GAGGTACTGTCTAACATGCTGGAACTGAAAATGGCAAGCAAGACATCCCTA
 CCCTGAGGAAACTGTAATCTAGTCGGAAATACAGATGTCAACCAAGTCT
 CACACAAGAANATTGTACAAAACCCCTAGGA

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GGAAAAACCTATCACCGCCTCTATGGAACCTAAAACAAAAAGAAAAGTA
 ACAAAAGGAAATGAATATTCATTCTGGAAAGAACATTGAAAAGAACAGGA
 AGAAAGAGAAAGCACAACCTGAACTGTCCACTAGAATTGACAACACTCTGA
 CAGAATGTCTGAACCTCATCGAAGGGTAAAGTGAACCTAAAGCTCCTC
 CAGCTTGGCCAAGTCTTATAATTTTAAACATATTCTAAATATAAT
 ATAGGAGAGATAGCCTCATCTAAGTAGAAATTAGCTACTCTGTAAAT
 ACAGAGTAATAATAATAATGACATGCCATAAACAGTGTCTTGTAT
 CTGTGCTTATAAGCACTTAGCTAAGATTATCTCACATAATTATCATAA
 CCACTGTTACTATGACCACTTACAAACAAACTGAGGCAAAAGAAGTT
 GGAAAACTAATCCAACAAACTGGCTCCAAAGGAACCTTGCTTCTTG
 GGTATCAAGTCTGAAGAGTACACATTAAACATTGAAACTGAGGTAGAA
 GGCAAGTTCTATGTAAGTTGGAGTATTCTGAATACTCTGGTAGCTAC
 AAATAGTATTAAATTATCTGGATTCTGCAGATAAGGATAAAATAGA
 TGGTAGGCAAAGAGTATGATCCTAGGAGAAATTTCCTGAAGGAAAAA
 TATATTAATAAAAATGATGGAATAAAACTCTAAGATCCTGCCTAGAGC
 AAAACTCATTCAAGTCTTGGCTGGTAATGTTGAACATCAACAAAAAA
 GGAAAAGTTCAAGTTAAGTCTACTCCAGGCAACATTTCACAACATCCAG
 TTAAATATTAACATATTCTCTTGTGGAAITGAACTAGAGTTCTTTCT
 TATCCTCTTTGGTGTGTATTATTTAAAATGAGTACCTTTTATT
 ATTGAAATCATTCAAGTAATGCAGATAATGATCAGGCCCTCTCCCTGTA
 CAAACATACACACTTAGGCATCCAAACTCTCTGGAGGTGACCACCA
 TTGCCAGTCATTCACTCTGGTTCTGATGCATGTCCATACAGTATAGGTATG
 TCGAGAAATGAAGTATTATATTGTGAGTTGCAATTCTTTATTCA
 TTTTGTGTACTTTGGTGTCTTCTGTGTTTCTCTAGTACCAATGTT
 ATGCTGACTTAGGCAGATGAGTTGAGTATTCTCTTGCCTATAAAC
 TGAAAATAGTTGTATGACATGAGAATTATTTTATTGTGAGGTTG
 ATAAAAACTGCCATAAAATCGTCTGGACCGGTTCTGAGGATGCC
 GTGTAGAGCC

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CGCTTTAACCTGGCTACCAATGGTCGTCAGTTCTAGATTCTCTATT
 ATACCTTTCTTGTCTTCTCTGGTCTGTTCTAGCCCCGAGTCTCT
 TAGATCTGCTCTCTAAATATTCTATTGACTTTACTCTCATTTCTAAGTCT
 TTATCCTTTGCTTACTTTCCGAGAGACCTGCTAACCTTATCTCCAA
 CTCTTTATTGAATTCACTTCTTACTATATATTCTACTTTGAATA
 CACCTCTCTTCTCACATTCCCCCATAGTATTGTCTCAATTGA
 CAGTTCTACTATCTTACTCTGGAGATAATAATAGTTTAAATT
 TTTATTATTATTCAAAACAGTGTCTACTCTGTCACTCACGCTG
 GAGTCAGTGGTGTGATCATGGACTCTGCAGCCTGATCTGAGCTCA
 AGCTATCCTCTGCTTCAGCCTCCAAAGTAGCTGGAAACCACAGGCATGTG
 TCACCATACCCAGCTAATTGTTGTTGAGGTGGAGTCTCACTCTGT
 AGCCCGGTCTGGAGTGCAGTGGTCAACTCTGGCTCACAGCAACCTCTG
 CTCCTGGGCTCTGGTCAAGCAATTCTCTGCCTCAGCCTCTGAGTAGC
 TGGGATTACAGAAACACACTACCAGTACCTGCCAGCTAATTGTTGTATT
 AGAGACAGGGTTTACCATGTTGGCCAGGCTGGTCTGAACTCCTGACT
 TGTGATCTGCCACCTTGGCTCCAAAGTGTCTGGGATTACAGGGGTGAG
 CCACTGCACCCGGCCACTAATTAAATTGTTAATAAGACGAGGTCTT
 GCTATGTTGCCAGTATGGTCTGAACTCTGGCTTAAGTAATCCTCT
 GCCTCAGCCTCCAAAGTGTGGGATTACAGGTGTGAGCCACTGAATCTG
 ACATTAAAGTTCTCTCTTACCAAGTCTTTCTCCCTTCT
 GCTTTTGGTTGTTTATTGATCTCTATCTGCTAGAAACTTCTG
 CAGACGTTAGTAATACTAGATTGAGAGTGGCAACTGGAAAGCTGA
 TTGGAAACTCTGAATACATGGGTGAGGCTTGTGGCTGTGAGTGTCA
 TTGATGTCCTGGCAAGGCCAATGGGTTGGGACCCCTACTATTAGTATA
 GGCCTGATCCCTGGAAAGGCTCTTGTGATCTCTGCCTGGAGGATAAA
 GGCCTGGCTACCAAGCCTCTGTGTAAATGTGAGGGAGAAGGGCTGGAGT

ATTCACATCATGCTGAA.CCTTCAA..ATCATCTGTTTAGTAATC
 TCCTACCTAACCTCTGCTCTGCTAGTATGGGAAAGATGACCTGAAA
 ATCTAACCAATTATTTCCCCATTAATATCATTTATGATTATTAGA
 AGTTAAAATAATTGTCACTGCTGCCTCCAAAAGACTGAATCAACTAGCAA
 CAAATAAGAATTTCACAGCTGCGAGCATTTAAAAGAAATAGCTT
 ATTGAGCCCAGGAGGTCAAGGCTGAGCTGTGATTACACCACTCTA
 CCCCAGCCTGGGTGACAGAGCAAAACCCCTGCTCAAAAAAGAAATTAAG
 GAACAGCTTATTGTTGTAAGACATACAATAAACAGAGCACATATT
 TAAATTGTCAACTTATACTTGATATAACCTGTGAAAACATCACCACA
 ATCAAGATAGTGAATATATTACACCTCTGATACAGTTAGCTCTGTG
 TCCCCACCTAACGTCTCATGTTGAATTGTAATCCCAATGCTGGGGAGGG
 GCTTGTGGGAGGTGATTGAATTGTTGGGGTGCACTCCCTGCTGTT
 CTTGAGATAGTGAATGAGCTCTCATGAGCTCCCTACTCACTCTCTT
 CCTGCTGCCATGTGAGGATGTGCTCCTCTTGCCTCTGCCATG
 ATGTGTTCTGAGTCCTCCCTAACCATGCCCTGTACAGCTGCAGAA
 CTGTGAGTCAGTAAATCTTTCTTCATAAATTACCCAGTCAGGTG
 GCTCTTATAGCAGTGTGAAAAGGAACTAATATACTCTAAGTTACCTC
 AAGCTGTTTAATTCTCTCCCTCTTCATTGCCAAGCAAACA
 ACCACCTGTTCTGTCACTATAGATTAGTTACATTGTGGGTTTT
 TTTTTTGAGACAAGGCTGACTCTGTTGCACAGGAGCAGCAGCGTA
 TC

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CGCGTTATAGGAGATGCGAACCTAACGAAATGATGATAAGGAGACTTTATT
 AAATATAATTGATTATTTGCATTACAGAAATTCAATTATTTAAA
 ATTCTATTCTAACATTAAATTCATCTGACTTCCAAGCTTAGCTTAGAAT
 CCTTCTGCTGAGGATTAATTAAATTGCTTTATAGGCCTTATCTA
 AAATCCAAGAATAATTGCCAGAACCTAACCCACCTCTAAATCTGTAAGTAG
 AAATTAGCTTTTAAATATGCAATTCTAACGATGATTAGTAATAAAA
 ATAATAAGATGTTAGCAACCTAACGAACTGATTGAAAGGTATTCT
 TACAGATATAAAACAGTTGGTTAATAAGAGAACATCATTGAAAGGCC
 AGTATGACATTGAAAGTAGTTAGTTAGTTATTAAACCAAGAAAAGCC
 TCAAGTGAACCTTAGTCCCTTGTAGCTAACATTATTGAATGCTTACT
 GTGTGCCCTGATACCTCTGACTTGCATTACCTACTGAGTCCTCACAAT
 CTTATGAGGCTACTATTAGTAGCCCCACTTACAGATGAGCAAACTAAGT
 CACAGAAAGGTTAAATAGGTGCTAGCTATTAAAGTGAACAAAGCTGAGAG
 CCTGTGATCTAACCACTTGGTATGCTGCCATGAAGTTAAATAGCTCAG
 TAGTCATTAAAGAGAACATTGCAATTGAAACCTTCAAGCCACTAACAA
 GTATATGCTTCTAACATTAAATTAGCTACATTAGATAGAATGGTAA
 AGGATCCTAACCTAAAGTTAAATGGAAGAAATTAGCCCTGAAAGAG
 GCACAGATTATCTCATCTGCAATAAAATCTCACCTTAGTTAGTTTAAAC
 ATAGTTTATCTGTGTTGAAATGTAACCTAAACAGTGTGCTTCTGAAAG
 TGAAAAATTCTCACTGGTGAGAATTAAAGTTAATGATTACCAA
 ATCACTTCAGTCATATTCACTGATATGCAATTAGACATATAAGACATATA
 AGTTTTATCTGTGTTGAAATGTAACCTAAACAGTGTGCTTCTGAAAGTG
 AAAAATTCTCACTGGTGAGAATTAAAGTTAATGATTACCAAAT
 CACTCAGTCATATTCACTGATATGCAATTAGACATGTAACGATGAAATA
 TGTTGTATGTACATGACATCATAGACACTGTGAAGGATAGCAGGAAATG
 TATATAAGGCAAATTATGAACAAATGGTTAACGTTGGGAAGCAGTGG
 GTTACACTTTACTTATGCAAGATTGAAACAGTATAGTATGCAAGTCTA
 AGGAAAAATCTACTGGAAAGGCCCTCATTCACTGACTTCCAGAGGCTTCT
 CTGGAGGTGACAATACTGACTTCAGTACATCAGCTGTAATGAGGATG
 ATACCTACCTTATCTGCTTACACAGTTGAAAGTAAAGTGAACCTCA
 GGAAGGAAATTACAGAACATTAGGAGAAACTAAAGCAGCAGTGAATAAT
 AGTCATCATTACAGTTATATAATGCTTGACAAATTATATAACACTTCGA
 TACATGACAACAATAACTAACACCCAGACATGTTATATACATTACCTCA
 CTCAGAACACCATGTGAGGAAGTTGCCATATGCTTAAATGCTCAAACC
 AGGACACTTTGAGAGTAAAAGCAGTACTCTTGACCAACAGGCATAAA
 TCAAAACTATCTGTGAAACCGGGATATATGGCATCCTCCTAGATAAT
 AGATACTTTACTATTAAATTGCTGTGAATCTAAACCTGCTCTAA
 AAAGTTAATTAAAGTAATGAGTACTGATACATGCTACACATGGG

FIG. 3 (6 of 52)

8/118

TAAATCTTGAACAGTTAAGCTAAGTG...AGAAGCCAGACAGAAAAGG...
 ACATATTACATGATTCCATTATGACACATCTAAAATAGGCACATCTA
 TAGACATACAGAGACAGAAAAGTAGACTAGCGGTTGCCAAGAACTGCAGGG
 AGCAGAAGATGGGAGTGAUTGCAATANGAAAACGCATTACGT

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TGAATCGCAATGATATGTGCCACTTGCACCTCTGTGACATATATAATT
 ATTTTAATGCATTCACTTTTCAGAGTCATTGTTGAAAACATA
 GACGGGAAATACTGGTAGTCTCCTTGTCAAGTTAGAAACACCCAAACAAT
 GAAAATGAAAAAGTTGCACAAATAGTCTCTAAAACAATGAAACTATTG
 CCTGAGGAATTGAAGTTAAAAGAACAGCACATAAGCAACAAGGATAA
 TCCTAGAAAACCAGTTCTGCTGACTGGGTGATTTCACCTCTCTTGCCTC
 CTCATCTGGATTGGCATATTCTAATATCCCCTCCAGAACTATTTCCT
 GTTTGTACTAAACTGTGTATATCATCTGTGTTGTACATAGACATTAATC
 TGCACCTGTGATCATGGTTAGAAATCATCAAGCCTAGGTCAAGCACCTT
 TTAGCTCCTGAGCAATGTGAAATACAACCTTATGAGGATCATCAAATAC
 GAATTCACTCTGAATGACGCCCTCAATCAAAGTATAATTGAGGCCAATGAA
 TCAGTACCTCACGGCTGTCATTACATAATCTGGATGAAGCAGGTACAT
 TAAAATGGCACCAGACATTCTGTCACTCCTCCCTCCTTCAATTACTTA
 TTTATTTATTCATCTTCTGTTGAAAAACATAACCTCTTCAGAGTT
 CTGGTTGCACAATTCTCCAGAAATAGCTGAAACACAGCACCCCCATAA
 AAATCCAAGCCAGGGCAGAAGGTTCAACTAAATCTGAAAGTCCACAAG
 AGAGAAGTTCCATCTTGAGAGTAAAGGGTTGTGCAACAAAGCTAGCTG
 ATGTACTACCTCTTGGTCTTCAGACATTCTACCTCAATTAAATTT
 CTGAGGAAACTGTCAGACATATTAAATGATTACTCAGATTACCCAGAA
 GCCAATGAAGAACAACTCTCCCTTAAAAGTCTGTTGATCAAACACTCA
 CAAGTAACACCAAACCAAGGAAAGATCTTATTATCTGATAACATATTG
 TGAGGCAAAACCTCCAATAAGCTACAAATATGGCTAAAGGATGAAGTTT
 AGTGTCAAAAACCTTTATCACACACATCCAATTTCATGGCGACATGT
 TTTAGTTCAACAGTATACATTTCAAAAGGTCAGAGAGGCAATTGG
 CAATAAAACAAGCAAGACTTTCTGATTGGATGCACTCAGCTAACATGC
 TTTCAACTCTACATTACAATTATTGTTCTATTCTACTTAAT
 ATTATTCTGCAATTTCCTCAATTGACATCGTGTATGTATTGCCATT
 TTTAATATCACTAGACAATTCAATCAGGTTGCTACGTTGGTCCCTGGGT
 TTACTCTAAATAGCTTGTGAAATATCTTGATATATTATTGTTTT
 TCTCCTATCTTGTAAATTCTTGTGAGCACATCCCAAAGAGGAATGCCCTAGA
 TCAATGGGCACAAATAATTGACAGCTTATTAAACATTATTCTGTAAAG
 TAAAACACTGAACACTTTCACTGATCACTAGCAACATAAGTGTATCAG
 CTTCCCTAAACCCCTCCATGTTAGGTCAATTGAACTTATGATCTAACAAA
 TTACAGGGTCTTATCCCCTAAATGAAATTATAAGAGGATTCAACACTTATT
 CAGCCCCGAAGGATTCAACCTGAGAAATTCTAAAGAACATTAAACCAA
 GTATTACCTGCCTAGTGTGAAAGACATTGTGAAGGACACAAAGAT
 GTATAGAATTCCATTCTGACTTCCAGGTATTACACCATAGGTGGGGAC
 CTAACACACACACACACACACACACACACACACACACAC
 CATGCACACACAATCTACATCAACACTTGTATTATCAAATACAATGAA
 TTTACTTCTTTGGTCTTCTTCACCACTGAAATTGTGACATGGGTG
 CTTATAAGTCATCAAAGGATGATGCTAAATTACCGTGATTCTAAGAATC
 TCAAAAACCTCAATTGTTGTGACTGCGCAAGAAGAAAACCACCCATGCTG
 CTGAAAGTCAGTTGTCTTGTCTCCAACTTACTCTTACCTCTCAT
 ATGTTGTGAATAAGCCAATAAGCAGACNCCTCTACAAAGTGAACCTG
 GTCTCTTCTCCTAACAGGG

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GTCTTGTAAACACAGGTAAGACGAGTTCAAGTTTATTCTGNNTTTAGA
 ACGGTAGTGAAGCGGTTTTCAGCNTGAGACCAACACCTAAGGTAAAGTAGCTG
 AATTGGGTTTGTCTTGGCTAAAGTTAACAAACCAAGCTGGTCTTAATT
 CTCCCTTACCAATTAGAGCACTCAGTAATCATATAAGTTGTGATCATTCA
 TTTGCTTAACTGTTGTTCTGTTTATTGCTGTTCACTGTTTCC
 CATTGGTTGACCTACTCTATGACTGATCAAATCCAAGGAAATT
 CCAAATTATGGGAATGAGGCCTCTGAAGTGGCTAAATTCCCACCCCTCCC
 ACACACACAAACGTGGTATGGTGGGGAAAAACGGCCAGCAAAAGAAAA
 AAAAAGGAAAAGATGTTGACCAACGGGCTTATTAC

ATAACAAGGCCACCTT...GCTAGCCA .CCATACTGAAAGAGCAATGC
 TGTTCCCCATGCTGTGGGTTCCATAGCTAACGTTCTGCCTTTTCCTA
 CCACCGACAGCCTGGGTTGGCTCAAATCAAGCCTTTCTGGTTTGATA
 CTTGGTAATGCTGAAATAGCAGCAATTGCTTAGCTGAAATATCGTAAT
 AAGATTTAAAAGATTATTTAAAGGACCTCAATAGTTAAAAGTCAGCT
 TAATTAAAAGCTAACATCCAAGATGTGTGATGTATGTATGCGTC
 GTATTAAAATAGCCCTCATGTTTTCTCTGTGACTGGATTCTGTT
 TTTTGAGCAAAGTTTTCTCTGTGACTGGATTCTGTT
 CATTACTCTGCTGTCTCCTTCTGCACCGCTGCTGAGA
 GCCCTAAAATAGTTATAATAGCCTGGGTTCTTAAAGAAAATGGAGAA
 GGTGCCAGGCTCCCTTCTGGGAGAAACTCTATTTCTTATGGAATC
 CCTAGAGTGTAAACAGACAAGTTCACTCAGCTCTAAACTGCTTGC
 TGTGTTGTGTTACCTGATTTTTGACTATTATATTGACTAGCTATT
 GCAACAGAAGCTACTCTGGGTTCAAGGAAGATTGTAGTTAGACATG
 TAGAAATGTCTTTAAAAAAACAAACTTTTTAAGTGCAGTGTAA
 AAGCATCATATGGTCTAGCCTCTAAATAATTCTCTTTGGAGACCAG
 GATTAGGGTGGGCTCTGCCAGAGCTCAGAGATCCAGTTAAAAGAGAGG
 TAGTCGGCCGGCGTAGAGGCCAGCCTGTAATCCAGCACTTGGGA
 GGCGAGGCGGGCGGATCACGAGGTAGGAGATCGAGACATCTGGCA
 ACATGGTAAACCCCCTCTACTAAAATACAAAATTAGCTGGGTGTG
 GTGGCAGGTGCCTGTAGTCCCAGCCACTCGGGAGACTGAGGAAAGAGG
 AATCGTTGAACCCGGGAGGCGGAGCTGCACTGAGACGAGATGGCGCA
 CTGCACTCCAGCCTGGCGACAGTGTGAGACTCCGTCTAAAAAAAAAGAT
 AGGTAGACTCGATGTTGTCGTAACCGAGCAAGTTAGAGCAACGCCAC
 TTGAGACGAATTAAAGAGTCTTATCAGCCGGGACCAAGAGACGGCTA
 ACGCTCGAAATTCTCTGGCCCTTGGAAAGGGGTTGATTTCTTATG
 CTTGGTTAGGAAGGGGAGGGGAGCTCAGTTGCAACAATTCTACAGGAG
 TAAAACATGCAAAGAAATTAAAAGACAAGTGGTTACAGGGAAACAAAC
 AGTCCAGGTGCAGGGCTCTAAATCTATCATAAGATGTTAGGTATGGGG
 GCTCTGCCGGACACAAACTCAAGGCTTATGCTGTTATCTCTTGAGCGAA
 ATCCTGGGAACTTCGTACATTGCTGCTCAGTACCTTATCAGTTAATCG
 GACTCTTGATATGTTGGAGTCAGCGTACACAAGTTAACTCCTTGAGGA
 AGGGGGTGGGTAAGGAGTCCTGATGTTGTAATGAGGAGCGAAATC
 GAGTCCTCTGGCTTCAGCTAAGGGAGAGCTTATTCATGTTGAAACA
 AGGCTAAGTGTAAAGGGAGAAAGGGAGAGTCTGAAAACAAGGTTAGGTA
 TTACAAATGTCATAAAATTGGTCTCTTATACAGTCTATGGTAGATTC
 TTTCATCTTAATCTCCTCTAGCACCACAGACTTTCTCTGTAC
 CTTGAGATGTAATTGCTATCTGAATTTCGTCTAAGAGTTGTTCT
 TTAATATGCAAATTAGGGTTATTAGCTGACAATGCCAAAGTAGTGAA
 ACAAGTTATCAAGAACTGAACGCTAAGGTAGGAAAAAAAGCTTT
 ATGAATCTATAAGATGTAATTCTATTGGCATGCCTAAACGTCTATGTAT
 TTACGTGTTGTCACAGTTTCACTACTGAAAATATAGAGGAGTT
 CTAATTAAATTGACTTAAGACAATAAAAGCCTGTAATCAAATACCTTATC
 AGGAAAAGGAAAAGACAAGTCCTGTTCAAGTCTATATAACTTA
 AGTAAAATCTTAATAAAATAAGCTAGCTTAACTTAACTTGAATGTC
 AAGAATTGCCAGGGTCTGGGTTACAGAACTAGTGGGGTGCACTGGG
 GTGAGGGTTGGTGGGGGGNNNNACNNNNNCNNNNNNNNNNNNNNNN
 CCCCCCCCCCCCCCTCCCCCCCCCGCCCCCGNGCGGGCCGCCCCCCCC
 CCC
 CCCCCCCCCCCCCCCCCCCCCCCCCACACCGGCCCCACACGCCCCCCCC
 GCCCCCGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
 CCCCCGGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
 GCC
 GCC
 GCGCGCCCCCCCCCCCCCCCCCCCCCCCCAGCCCCGCCCCCCCC
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 GGCAGTACGCTATAATTCCCTCTCACCTAACCTCATCTGTTCTGATG
 GATGTAATTGTTAGTTCTAAATTCCCTTTCTGCTCTGGAG
 ATGGGTGATTGATGATGTTGCTGGGATTGTTCCCTCAAATCTCATGTTG
 AAATGTAATCCCCAGTGTGGAGGTAGGGCCTGGTGGAGGTGTTGGAT

FIG. 3 (8 of 52)

10/118

CATGGGGCAGATCCC ATGAATAGC :GGTACTGTCCTCTCAATAG .:
AATGAGTTCTCCGTGAGATATGGTGTAAAAGTGTGGCACTCCCCCA
TTGCTCTCTTGTACTGCTTCGACATGTGACATCCCTGCTCCCCCTCGC
TCTCTGCCATGATTGAAAGTTCTTAAGGCTCGCCAAAAGCTGAGCAGA
TGTGGGTGCCATGCTGTACAGCCTGCAGAACTGTGAGCCAAAATAACT
TCATTTCCATATAAATTACCCAGCCTCAGATATTCTTATAGCAACATA
AGAGTGGCTTAATACAGGCTGGCATGGCTGGCTCACGCCGTAAATCCCAG
CACTGTGGGAGGCTGAGGGGGTGGAACATGAGGTAGGGAGATTGAGACC
ACCGGCTAACACGGTGAACACTCCATCTCTACTAAAAATAACAAAAATTAG
TCGGGGCTGGTGGCTGTAGTCCCAGCTACTCTGGAGGCTGAGG
CAGGAGAATGGCATGAACCCGGGAAGCGGGAGCTGAGTGAGCCGAGATT
GCACCACTGCACTCCAGCCTGGCGACAAGAGTGAACACTCCATTAAAAA
GAAAAAAACAAAATTCAAACAGAACAAAATGAAAAAAATCCAAGTGAAC
GGCCCCCTATAAAACCCCTCTGGGGCCATCCTCCACCCCTCAAGTGA
AACACACATTAAACAATTGGTGCATATCTTCCAAACCTTTGTTGTACA
CATATAAAAACATACATGCTTTGATTTGGCTCAGACTGTACATAGTGT
TTCCTCTTGCATTTACACTTAATATATCTTGCATCTTCTATGTCA
GTGCATGTTGGCTCGATGATATTCTATCAAATACCCCTCCAAAATG
GTAAAATCATTTAAAAAATCATTACACACAAGTACATATTCAAATTTA
AAAGAAAACAGAACATCCAAAACACAACGACAAACCTCTAAAATAATCTC
TATCTTCCACCAAGCATGGAACAGTCACTCCTTTCACATAAAACGAA
TTATGTGATTGGAAAGATTAACCTAACTACACATTATATACAGAACATG
TTCTATTGTTAACGCCTATCTGAAAATAAAAATTCAAGATGATTAATTCA
CTTACACTTAGAAATTAGTCAATATACTATGAATACACATTGTGATCAG
TTATAATATGATGCTCTTAGTCTAGGGTTCAATTAAATAACAGTAAAAA
AAAATTGGATAAAAGACAGCTAAACTGAAAATCCAGAAATTCAA
GATTATATTGCCAACTAAAACACTGCCATTACATTTTTTCTACTT
GGTAGCAAATGCTAATGGAATTCAATCCTGATTACTAAAGTCAGTTCAC
ATCACACATTCAATCAGGATAATACGAACATAATATGCCTACTATAGCGT
TAGATTAAGACATAAAATTGGCTGTGAAAGTAATGACTGCGTACCA
TTGAGACATTGTCACCCTCAGCACATTGTTACGAGTGACTGGATG
TCCACAAGGATAAAAACGACAGCAATATTCTATCCATACAGATTG
AAAGCTTCTCCTCTTGAGGTGTTAGCTGCTCTCAGTACTAATCTC
TTCTGCAATGAAGTCTGACTGATTGCTCTGTGACTGTCTTCTGAGC
CTTCACTGGATCTGCAATCAGAACCTCAAGTGATTTACAGTTGCTCC
ATGTCTGAATTCTTCTCATTATTCTTAATGTCCTTGAAACTGAAC
CCCATTCAATAGCTCTGTACCATAGGATTAGGAAGATGGTATCAAT
TTTCTAGTTAGTGTGGCGTTTTCAAGCTCTTACAGACACTCCT
CAAGTGAATGGGATAAATGAATATTGTTATATATTTCGTGCTCTGT
TCTAACAGATATTACACCCCTGGATGCCATTACATGTTGTCCTCAAGGGT
CTNCTGGGCT

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CTTCTCCCTTTACCCCCATTTCGTAGGGATTGGTAAAACCCATG
TAAAAAAATCCAAACACCCGGCGGGGAACGGGGGTTCAAGCTCGTATCCCCA
CCACCTTGGAACCCAAAGGTGGCAGGATTGTCGGAAGCCAGGCATTGAG
CCCACCCCTGGGAAAAAAAGAGAACCCCCATTGGTGAACAAAAACC
CCAACCCCTCCAGGAAAGAAATAAGTATGGCTGGGTTGAAGTCACCAAG
ATGGCCGACTGGCTGGTCAAGTAACCTTACCTGATGGTGTAGAATATT
TACCTTCACCCAGGTGGAGAATTGCTTGAGCCAACCTCAGTGTGGATT
CAGGAACCTGATTAAATTGGTATCGTGAATTGGATTAGATTCTCAGGG
TGCATTCACTAAGTAAAAGTGATAATAGCTACTTTAAGTAAAATAATGA
ATGAATCAAACACTCTAAATCCATGGTGTATGCTAAGCTCTTCTGTAT
TTTATCTCATTGATATTACAAATATTGATGTGTTAATAGTAATGACTA
TCTCCATTAACTACAAGTAAGGAAACTGACATTGAGAGATTAAAAGACTAG
CACAATCACAAAGTAAATGAGATTGAATCCGGTCTGATTCAAACCTC
TACAGTATTCTAAATTCAAGGAGACTAAATTATAAGATGGAGAGCCAATT
TTACCTTATAACAGGGTTAGAATGGCAGAAGAGACCTGACATTACACCT
CTAGCCAGTGCATCATCTCCTGTAGGCAAATATGCAAGGAAATCTATAAT
AAGAACGTCTTGGTGAAGGCCAGGTGCAGGGCTTACACTGTAAATT
CAGCACTTGGGAGGTCAAGGTGGAGGGTCGCTGATGACAGGAGTTG

FIG. 3 (9 of 52)

11/118

AGAACAGCCTGGCAACAATAGTGAGACCTGTCTCTACAAACAAAAACAA
 ACACAAAACAACCTCAAGAAAACCTCTGGTATGGATCAGAACAGATG
 AATTATCTATCTGATCCAATGCTTAATGACATTAAGCCACAGTCCACTC
 ACTGCCACAATAGAGATATACTGCCAATGCCACTCAGGTAATCCCCTCA
 AAAGTGGTAATGAGGTCTGCAGCATGACTTGTCTTAGTGTATCCCAGCCT
 GAGACCTTGAGATTGCAGCATTATTACATATGCACAAAACATCTGT
 TGAAAAATCTCTAAATTGATGCAATACATTGTATCAAGAATACCTGTC
 TGTAATCTCCATAAACCTCTCCTTCTGTTTAAAAAATAGAACAGCA
 TTTCTCCTTACATGACAAAGAAATGACTTCACCATCTACGAAATAGTGA
 TAGGAGCTGTGGAAGGAAATTAGCTACTTCTTGGAGATGAGAA
 GGGAGTGTCTCTGAAAATCAAGGCTTGTCTGCTAGGAGCCAAAGT
 CGTTTTTAGAGTGTGGACAGTTGAGAAGATAAGACAGGGACCATCCACT
 CATTTTCTTATTCCATAGGCCCTCTCAATTGGGAAAGCAGTCCAG
 ACCTTTGGAAGAGTGACACCAAAGGCAAGCACCTGCTTGGCAGGCCCT
 CAGCTTCTACGCAAGTATAAGTGAGTATATAAAATGGGGTACTTGTGCT
 GTTGAGTACCTTATTCCAATGAGGCCCTGCCGTGCCCCGTGCTG
 AGAAGGCCTCTACTGGATAGGTGGAAGTTGTGTTCTCATTTTCTAA
 CCCTGGATTGACTTGCCAAAAGGAAGCCATTATTAACACTATAA
 CCATCTTAATCTGGGACTCTCTTCATGCAGTGGTCTTAACCAAGTGATA
 AACATGAGAGTTACTTTGGAGCTTAAAAAATTAAGATGCTCAAGGTCT
 ACCCAAACACTGACTGAATCTCCAGAGGTGAGGCCAGGGATGATACTTT
 GAGCCAGACCTCAGTTACCTGCAGAGCTCATAGGTTGCATAACACCC
 TTTGTCAGCCACTCTGATGAAAAGAAAATTGGTGAGGAATAAGTTTAG
 AGAAGAAGGAGCAAAGGTGTTGGCCAGTGAGAGCCAATGACAGGGAA
 ATGCAAACAATGTATCCACAAGAAAGGTAATTACCCATAGAGCATT
 AGGATAAAATGAACATCTCATGCCTAGGGTTGAGAGAGGGTACAAAAAAA
 AAAAAAAAGACCACTCTGGATACACAACCGATAAAATGGAATAAGAA
 TTTTCCTGTAAATTAAAAATCCTTGTACTGAGGTATAATTAA
 TCTATTATGTATAGTCAATGAGGTGTTAGATAATAAATT
 GTAAATTATTATATTGTATACATACATACATTAAAGTCAGA
 AATGTATATAACCATTAAACTTATAATCATTCACTGAGATATA
 GATACACGAGCATATTATCCACCACAAATTACCATCTCAAC
 AATTCCATCCCCCTCAATTTCAGCGTAGGGTTTAAATGTCAAAG
 GAGTCTACTCAGTGGAGAAAGTTAAGGAAAAACCTTGGGCTTGG
 GCTCCTTCCCCCTGGGTTAAAAGGCAGGAAATTGGGCTTACCCCCCT
 GAAATTGGGAACTGAAATTGGGAAGTTAAAAAAAAAAAAA
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TCAAGCAGCTTCTTCCATTGGCTTCCAAATTGTTGGGATTACAGGCAT
 GAGTCAGGATTCTGGCTTAGTTACATTCTAGAGTTGTATAATG
 GAAACATACAGAATGTATTTCCTGGAGTGGGGAGTGTCTTCTATT
 TTTCTTCCATTTCCTCCCCCNCCTGGAGTCTCGCTCTG
 TCTGTTGCCAGGCTGGAGTGCAGTGGTGGATCTGGCTCACCGCAAGC
 TCCACCTCCGGGTTCAAGCAATTCTCTGGCTCAGCCTCTGAGTAGCT
 GGGATTACAGCGCCGCCACACCTGGCTAATTGTTGTATT
 GGTAGAGACGGGTTTACCATGTTAGCCAGGATGGTCTGATCTCTGA
 CCTCGTATCTGCCGCTCGGCCCTTAAGTGTGGGATTACAGGCGT
 GAGCCACCGTCCCCGGCCAAGTGTCTATTCTTAACCAGCTTCA
 CAATCTTTTATTACCATCTGTGATCCCCTCCAAAGGTACTA
 GATGTGATGGTCTTAGGATCAGCTACCATTTGCCAACTGTTCCA
 GCCTTCAAAATTCTTCTTCTTCTAAAGATACTCTGTGTGAGG
 CTCAGAACTCTGAATTGCTACTGCAAATATGAACCTGGTGTGAATG
 CCAGGGATTGCTGATTGATCAAAGAAATGTATCCCCTCTCCCTACT
 CTTGCTGCTCTCATTTGTTCTTCTTCTTCTTCTTCTTCTTCT
 AATATCCCCTTAATGTTATAATTAAATGGCTTGGCGAAAAGTACA
 GAATTAGGTGCAAGAGTGATAGCTGTTATTCTTCTTCTGAGA
 CTGTTCATATATGCAAGTTATTAAACAGAAAGTTCTGCAGTGACCTGAGA
 TGTCAGGGGGTCTGATAGAGTACGTTGAAGGCAGTTACTGGAAAAA
 TAATGCCATTCTGGTTGTACTTCGGTAAGTTCAGATGACCCAAATAT
 TGTTACATGTGGCATTCAAGTAAAGTAGCTTCCCCTCCCTTCT
 TCCCTTCTCCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT

TAGGAGGGAGAGCTTGCC...CCCCGTGG...ATGGAGAGGTCTTGCAGAGA...
 AAAAGAGATGCTCCACTCAATGCAGGATGGTGTGGAGGTAAATGGGAT
 ACGTCTGGCATCACTCAGGAATGGCCTTCCTGGCAGGGAAAAAGGGAA
 GGGGAAAGAGGAAGGGATTNNANATNAATTGCTGAATACGGGGATTCC
 ATGGCCTGGATCCAGGAAGAGAACCTTGGGAGGTGTGAACCTGGAAGGCA
 TCANCTGATGAGGAGCAGCCTGAACCTCCGGGAGGACTGTTTGGTGG
 CCCGAAAAAAATGCCCTCCACACACAGGGAGGCCACCCGGCTGATGGGC
 TGGGGTTGGACGGACAGCCCTAGGACAGGTTGGAAACCAGGCTCAGG
 TAGGGCCTGCCAGGGTCTCGCTCGTCTCTTCTTCTGGTCTTAGAAA
 ATAGAATCCAAGGCCTTGTAGAGTGAAGGTGGTGGAGGGCAG
 ATGGGCTTAGGCCAGGACACCCGTAGAGTACTGCCAGCTGTCTC
 AGGGACTCTGCTGAGGTCACTCCAAGGATCATTCTAGCCTGCTAGACA
 GTACTGACAGAGGGAACCGTAGTATGCACCCACTTCCCTCTTTCAAT
 GAAAGTTAAAGGTACCATTTCTGGCAAAGGAAGTTCCACAAATAT
 TCCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCAAACCTCC
 TGTGCTGGGAATTCCAAGGAAGTAGGGCAGAGTTCTGGTGGAGACAA
 AGTGAATTCCGAGTGATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCAGTA
 GCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGCAGCAGAAC
 AGAATTCCCCCACGTGTCAGGCTCTCATTTGCCAACTCAGTCTCTA
 AGTATTTTATTGGCAGGAAAAATAAAATAGCTATGAGTGAATAATTCA
 TTAGACCTGAGCCTCCATCAATTGTGTTAAAGGCTGACTCTCTTAA
 CCTTCCCTGGATGGAAGATGCAAATGTTCTGATCTCACTGTAAAAAA
 AGAAGAACAGTGGGTATATTGTATGCTTGAGTCCAGCCATTAGTCACA
 AGACATAGAGATGACTGCCATGTGTAGACTTTCTATAGACTGTGTGCT
 AAACCCGACCTGCCACTTCAAGGAGTAGATGAGGAATGTCATGGTCT
 GGGGAGCCCTACCCCAATTGGGCAGACATTCCAAGCTCATTTCTGT
 GGAGGGGGTTGATGGTAAAGGAACGGCTGGGATTACTCTTCTTCTAG
 GGCCAAGAAAATGACATGCTGCCATGTTAATCATCTTCCCCCTGT
 TAATAACTATGGCTTTAAGTCCCCGGTAGGGCCTCCTCCAAAATTGGG
 GAAAAAAATTCCCCCTCCCCCTAAAAATTTTTAAAAAAACCTTT
 TTTTTGGGGTTGGGAAAAAAACAAAAATTTTTCCCCAGGGGTTT
 TTTAATTAAATTCTCCCCAAAAATTGTTTTTTCCCGGAAAAAA
 AAGACCCCCCCTAAAAAAAGTTTTGGCGGAAAAAAATATT
 TTTGTGTTAAGAAATGGAGAAGAAGGGGGTTTTTTCTCTCCCC
 CACCCGCCAAGGAAAGGTTGTTACAGATTGTTGTCTCCGCCA
 T
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ATGTGCTGCCAAATCATCTTCCAGAAATATTGCCCTTCTTGT
 ATAGAGTGGCACTGCCCTATATGGTGACCAATTGCCACATGTGGCTGTT
 AACACTGAAATTGGCTGTCAGAATTGCAAGTGTAAAGTGTAAAACACAT
 ACCAAATTCAAAGACATGGCACATAATAAAAATGTAAAATATCTCATT
 AACAAATTATATTGACTGTGTAAGTAACATTGAAATATATGGATTA
 AATACATGGATGATGCCCAACACCCACAGTCCCTATCAAGTCTCTACT
 TCACATTTGACTCTGACTTAGAAATAGCACTGGCGTCAAGAGCCT
 ATTAATGTCGTCATAAGGTTCTGGGACCCACAATTAAACAAAATGAC
 ATATAAGAAAACGAATAACATTGAAACAAATGACATTATCGAGGACCTG
 CTGCATGTTGTTCACTTAAAGTCAGTGTCAAGAAACTATCAGTACAT
 TTAGTGAGGAATTGCTGCTCTGTTACAGGAACCTGGCAAGTTAC
 TTAATTCTCTAAGCCCCGTTATATCCCTGCAAAGAGAGAAGGATAATA
 ATCACCACTACTTAGTGATGTCGTAAGGAGAAAATAAAATAATATG
 AAATGGCTGACAGTGTCTTGTCAACAGAAGATGTTGATCCACAGTAG
 CTGCTATTGCTGCTCACTTCAGTAGTAATGGTCCAGGGAGGCCTTAA
 TGTCATGGTGCAGTACATTCACTGTTGGACATGGTGAAGGGAAAGAC
 CAGGCTCATCTAAACACAATAGGATGCTTGTGGTTTGAGGAGGAATC
 AAGGACTAGTTATCCACAGCTGTAACATGCATGGATCAAAGAGATAAGG
 CACACAAAAGACTTGTCAAGTAGCAAAGCATTACAAAATGCAGAGACCAG
 CTGGGGTGGTGGTGAAGTCAGACCCAGCTCCCTGTGCCTGGCTGAGT
 GGTCTGGCAAGTCAGCCATCTGCTTGTGATGCCCTCCCCATCTATAG
 AGAGGGAGCAACTGAGGCCCTTCAAAACTGAAGTCTTATTCTGCT
 ACTTTAGAAATATCCACATTGGTAAATTCAAATGATCCAATGATTCC

ATTTCTTAATGTCAAAAGCCCCAACATCTAAATGAATC
 AATAAAATTTATTGTATGTTGATTGCTGAAACTCTATTAGC
 AACACACACACACACAGAACCATAAGCCTCATCTTCTGGAT
 AAACGAGCCTCCTGCTGGCATTAAAGTCAGATAAGTAAATGATT
 CCAACTCGCCTTGCAGCAGTTCAAGATGGCTTCCCTGCGTGGCAGTG
 GCCCTCTGACTTATGATTCTGTGTGCGCTGTTACCACTGCAGCT
 TAAGTGGAAACAAGAACAAAACAGCCTCTGACCCCAAGAGACTGTTGG
 AGGCAAAGGCTCAGTCCAAGAACCTCACACGTGGGAGCCCAGAGGCC
 CAGCCCTGACCTTCTCAGTAATAACATAAGAAACAACAGGCAGTGGC
 CTTATTGGATACAAAGAGTGGTCTTCTTAAATCTCCTTAGTC
 AGGGTACCCCTCATGGACGCCAACATCCATGGTCTGCTGAGTC
 CCTGCTCCATATTCTGCACCTCTCACTTGAATATCCCTGGAGTACGT
 TAAGCAGCCAGGTTGGAAGTCTTGCTGTGAGGCCGGGTGTGCATGT
 CCTCTCTCAACAGGACACAAGCTCCCCAATCAGACGGTATGCCCTCA
 CGCCCCCTCCAAAGCCTCCCCAGCAGCACCGAGCATGTGAGGGAGCTGG
 GGCCCAGGCCATGATGGGAAGCACTCTGCTAAAGACTAGGGTGTGC
 GCCCTCAACTGTGGGAATGAGGCCAGCTCTGGTCTGCCCTGGTTT
 CCTCTGGACAATCAACATGAACCTCACCCTTATCCACTTGCAT
 AAACGTAAAATAACAAACCAGGGCTTCTGTACAGGAAAGGGTTT
 TTTTATAAGATTAACAGAGATGATTCAACACACCCAGGATATAACACAT
 GGGCCATGAGTCAGGCCAGGCATTGCTCTGGTCAGCTGTTGGC
 CCCCTGGCAGGGCTCTCCCTGAATCTCCCCCTCTGACTCCCCATCA
 CCACAGCACGTCAGCTTGGTACAAGGCCAGTAAATGGGAAGGGGT
 CAGATGACATAAGAGGCCCTTCTGTCCCATTGAAATATATTGGATAA
 CAGATGGCATTCCCCCTGTGCTTGCCAGGGCCAGAGCCTCCACTTG
 CTAGAGGCAGACAGAGGATGGAGAGGCCCTTCATTAGTGGAGGACATCA
 CAGGTGGGCAAGAAACCACAAGCTGCACTGAGGCCAGCCTGAAATAG
 CAGCACCTGCCGGCACCTGTGGCTGGGACAGGGTACAGGATGGAGGG
 GCCTCTAAGCCTTATCTCTATGTAAGTACAACCCATTCTCCAC
 CTCACAGGCCAGATCAGCCTCTGTGAGGTCTGGTGGCAAAAGGATAAT
 TGCTGCCGCTGCCGGTGGCTTGCTTGCTTGCAATTCTGGAA
 GGTTGTTGGGTTACTCTGCAATAGGTCTCTGACCAGCTACCCCTCTA
 CTGCAAACCTCAAACCAACTCAAAGAAGATCCAGCACC
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 CGCGTAGTCTAAAGACTGAGTCTGAAGCTGCCCTCTGCTATGGACTT
 CAGATTCTAGCCCACCTGAAATTGCTCCATATCCTCCAAGCCATGCCATC
 CCTGACTCTGGCTCCAAAGCACTTGTGCTGCCATCACACAGTTG
 AGTTAAGCAGAAAGACTGGTTCATGTAACACTTGTGAAAGCTTCTC
 ATTCTTATATAATCTCTGCTTGTCTACTGCTTAAATCTAGAAA
 TTGTTACAAACACAAAGGTATCTTAAAGCTCAAAGCTGATTGTG
 CACCAATATATACCACTCTTAAATGGCTCCATTAAACTTGTGAGAAAGA
 CTTTATGGAGCCTACATAAGGCCATGACTACCTGGCTTTATTCTCC
 TCATCCTCATCTCACCAACTCACTCTCCACTCCTATACCCCTCACTCTT
 CCCCTCTCTCTGTGAGCTCCAGACTCCAAATTACCTACTTCCACCCCT
 TTTGACCCCCAGGGACTATCTCAGCCTGGAATTTCCTCTTGCTCTC
 CACTGAACCTGCACTCCAGTCAAGACATGTGCTTATGTACACGCC
 TTACCGTCTTATCTCAGTTGTAATTACTCATTTAGAAAAGTGT
 GATGAAGGTCTCACTGTCACTGTCAGCTTCAAGGATAGCAGGAATCATAGCTGAT
 TTTACTTACTTAAACGGGTTTCAATTGTAACTTTTTTTTGAG
 ATGGAGACTCACTCTGCCAGGCTGGAGTCAATGGCATGATCTGGCT
 CACTGCAACCTCCACCTCTGGGTTCAAGTATTCTCTGCTTCAGCCTC
 CCGAGTAGCTGGATTACAGATGCCAGCACGCCAGCTAAATT
 GTATTCTTGTAAAGACGGGTTTCACTCATGTTGGCAGGCTGGTCTCGA
 TCTCCTGACCTCAGGCAGCCACCCACCTCAGCCTCCAAAGTGTG
 TTACAGGCATGAGCCAGGGCACCCAGCCACTCCTTACTTATGGGTG
 AGAAGCCATTAGAGATCATTCTTTCTCTTCACTAAGGCA
 CCAGGGTCACTAAGTAGTAGGATACTTGAACAGAAACTCAAGAAATTGA
 GTTTAATTACCTCACACTCTCATATGAATTCTCATGTGACCTCGGG
 CCATACCTCCCTGTACCCCTGTTCTTATAAAAGTAAGAGTTAA
 ACTAGATGGCTCCGACATGCATCCTCTCAACATATTCTGGAACCTTC

FIG. 3 (12 of 52)

14/118

AATAAACTAAGATAAAAG AGAATAATTAAAACCTTAATTAAAAGAACAG
 GGAAAGGAAGGAGTACATTAAGCAAAAGAGACATCTCATGGTTGAAGA
 AGTGTATGCCCTGGTCTGGATCCCATTAGGAAACTTGGTAACCTTGC
 AATCTTGGGAGATTGCTTAATTCTCTAGACCATGACTTCCTCTCTGT
 AAGATGTGATAAGAACATCTACCTCACAGGTTCATGAGAGGATAATG
 AGATAATGTATATAATCCCTTGACATGGTAGGCTTATGTTAAGTCC
 TTCCCTCTCTCTGTAGCTATCATGGAATTAAAAACACATTATAACTA
 GAGCATGAGTTGCGACTAAAGGCTAATTGCTCTGCATGTGTGGCTCA
 TGATGCTTATTCTCTGAAGAGCTTTATACCAAGTGAAAGGAAATAA
 TTGCAATTCCCTGAAAATTACAGGAAAAAGTTATGTTTCTCTCATT
 CAAGTGATTCTGTTAGACCCAACCACATGCAACAATTAAAGTTGCTTC
 CAAATATATTACAAATATTCTGTCTCAAGGAACAATGGCAAGACCA
 TGACTCAGGTCACATCCGGATTCCACCACTAACATGTACCCATTACT
 TCAGTCACCTICATTCAAGGTCTTACATATCACAGAATAAAATCAGATTC
 ATCAGAGGAGGTGAAGACAGGGAGAGGATATTCAATCCCTCTCCGC
 AACCCCCGTTTTTTTTTTAACAAGGATCCTAGAGTTACTGAATG
 ATAGCACGTTGAGGGGAAAGACCTAACGGATGATCTTATAAGCCATC
 ACTTGGTGTGGTGGTGTAAAAAAACTCGAGTATCTTATGCAGTGGAA
 GAGAAGATTGGACTCGGAATCAGAAGCTTGAAGCACTGGTTCAT
 CAGTCTGTGATCTGGTGGTCACTTAACCTCTCAAGGGTCTCAGC
 TGTGAAAGAAGATAGTACAGCTAATTGTATGTCAGTGAGGAGGCA
 GTGAGATAGTCAGGTAACATAAAACAATTGTCACATGAAACGCATCA
 CAGTGATTCTTGGACCCACAAGCTCAATCTTATAAAACATATCCAGTC
 ACCCACCAACATAGATCATCTCACCTTGATCTGATCTGATTGTGGATCAT
 GGGGAAAAACTGCTGATTCCTAGCAAAACCCATGGCATAGGATAAGTGC
 CAATAATTCTTCTAAATGATTAGATGACAGTGACTCATTAAGGG
 TTCTGAGGCCTCCTCAGAGTCGAGAGGTGGTGGCTGAAGCACC
 AGTCCCTGTACAGGATGGCTCCAACGACACACCAGGGCTGCCAG
 TATGTTCCACTATCTACCCAGTAGAGCCCTGCCAGTACGTTCACTGTC
 CCTTCCCTAGAAGAGGTGACTGTTCAAGCTCCAGAAAAGCAGGCTC
 CCCAAAACAATGCAAGGACCCACCTCTCTGAACCTCACCCACCC
 TAGT TTCTTAAAAATCAATTACAAGAAGATCATGTGAAGGAAAGGTTGG
 GTGATATTCTAACCCAGTTAGCTGTTCTAACCAAGTTCTTTGAAA
 AATTCAACAACCACCTTGGGAATTATTACAACAGAGGAGTGAGGATG
 GGACCAGGATAGGTATTGCTATGTTGGTGAACCAGGGTTTTCTG
 GATTACCAAAGAGATGGTATGCATTGCTCCAGAAGCTAAATATCTTCAG
 GCTTCATGGTGGCCTCACCTGAAAATGTTATCCCTGTTGAAGCTT
 AAGCCAGTATTCTATAAGAACTATATTCTTGGTGAACTGAGGCATT
 ATAATGATGACTATACAGGTTCTGAGTGACTGAAGCCATCATAGCATT
 GTCATTATTGTTAGTTGCACTCCATAGCAGCTCACATTACAATG
 TGCTTGCAATTGTCCTTAGCAATAGCCCTACAAGATTCTCAGGAGGA
 GAGGGTTAACCGGATTAACATTCTGTGAAGCCTAGCGAGATTACGC

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AAGAGTTTAAAATTAAAGTAAGGACGCCGGAAACAAATCAATCCCAGCA
 AACATTGTTGGATTATCATCAAGCAATTTCAGTTATCCCTGTC
 AAATACATTAAGTGTCAAAATTGGCATAGGGGAAACAAATAATAAC
 CCAGCCAAACAGAATAATCCCTGTTGTTCAATGTTGATAAAAAGAC
 ATTACTATTGGTGTAGGAAATTAGATACATCTTCAATTATTAGTAAA
 TTACCATACATTCTAACCTTGTGGCTTAGGCAGTCAGTCCACAGGCAG
 GAAGGAGGTTGGCAATGACTGTTATCATCTCTGTTCAAAGC
 TAAACCATAAACTAACGTTCAATTCTCCAAAGTTAATTGAGCATATGCCAGGA
 ATGAACAAGGACAGCCTGGACGTTAGAAGCAAAATGAGTCAGGTAGGTC
 AGATCTTCTTCACTGTCAGTGATGGCAGTTCTAACTTTAAATGATG
 GCTATCACAGTTTCTATAAAATACTAGATAACAGTTAAAATAAA
 TTAGGTAATGAGTGTGCGATAAAATTAGTAGACAAACTCACCATAATT
 AGAATCTAAAGTTAAATTAAATAATATTCTATTGTTGTTATT
 AAGAAAAACATATTGAGGAAACATTCTTTAAAAAAAGTGTCT
 TTAAAAAGGTGAATAATTGTCATAATTCAAAGTTATTGAAAAGTTA
 TGTATAAAACAAGGTAAAAGGAACAAGGAAATAAGGAAATGTAAGGAA

ATTATAGAAATAAAGTGATTTTTGGTAAGAAAGCTTAAAGAGAAA
 ATTTAGGTAGAAAGAATCTTACCTAAAATTTGTGCTAGAATAAAGTG
 ACTGGCTAAGAAAGGGATGTTCAAGCTATTATGACAAACCCACAGCCA
 ATATCATACTGAATGGCAAAAGCTGGAAACATTCCCTTGAGAACTGGC
 ACAAGACAAGGATGTCCTCTCACCACTCTATTCAACATAGTATCGGA
 AGTTCTGGCCAGGGCAATCAAGCAAGAGAAAGAAATAAAGGTATTCAA
 TAGGAAGAGAGGAAGTCAAATTTCTCCGTTGCAGATGCATGATTGCAT
 AITTAGAAAACCCCACATTTCAAGCCCCAAAACCTCTTAAGCTGATAAGC
 AACCTCAGCAAAGTCTCAGGATAAAAATCAATGTGAAAAATCACAGGC
 ATTCTTACACCAATAATAGACTAACAGAGGCCAATCATGAGTGAAC
 TCCCATTACAATTGCTACAAAGAGAATAAAATACCTGGGAATACAACCT
 ACAATGGACATGAAAGACCTTTCAAGGTGAAC TGCAAACCACTGCTCAA
 GGAAATAAGAGAGGAAACAAGCAAATGGAAAACATTCCATGCTTATGGA
 TAGGAAGAATCAATATCGTAAAATGCCACTGCCAAGTAATTATA
 GATTCAATGCTATCCCCATCAAGCTACCTGACTTCTTACAGAATTAA
 GAAAAAAACTAATAGCCAAGACAATCTAAGCAAAAGAACAAAGCTGGAG
 GCATTGTGCTACCTGACTCTAACTA TACTACAAGGCTGCAGTAACCAAA
 ACAGCATGGTACTGGTACCAAAACAGATATA TAGACCAAAAGAACAGAAC
 AGAGGCCTCAGATATAACACCACACATCTACAACCATCTGATCTTGACA
 AACCTAACAAAATAAGCAATGGGGAAAATAATTCCCTATTAAATAATG
 ATGTTGGGAAAATGGTTAGCCATATGCTGAAAATGCTGGACCCCT
 TCCTTACAACCTATACAAAATCAACTCAAGATGGATTAAAGATTAAAC
 ATGGCTGGGATGGTGGCTCACGCCGTAAATCCCAGCACCTTGGGAGGCC
 GAGATGGGTGGATCATGAGGTCAAGGAGATGGAGACCATCCTGACTAACAC
 AGTGAACCCCTGTCTACTAAAAAAATACAAAAAATTAGCTGGGATGGT
 GGTGGGCGCTGTAGTCCCAGCTACTGGGAGGCTGAGGCAGGAGAACGG
 TGTGAAACCCAGGAGGTGGAGCTTGCAGGGAGTGGAGATCACGCCACTGCA
 CTCCAGCCTGGGCAACAGAGTAAGACTCCATCTCAAAAAAAAAAAAA
 AAAAAAAAGAAGGATTAAACATAAGACCTAAAACCATAAAAACCATAAGAA
 GAAAACCTAGGCAATACCATTCAAGGACATAGGCATGAGCAAAGACTTCAT
 GATTAGAACACCAAAAGCAATTGCAACAAAAGCCAATTGACAAATGGGAT
 CTAATTAAACTGAAGAGCTTCTGCACAGCAAAAGAAACTATTGTCAGAGT
 GAACAGGCAACCTACAGAATAGGAGAAAATTTCATCTATCCATCTG
 ACAAGGGCTAATATCAGAATCTACAAGGAATTAAACAAATTGCAAG
 AAAAAAAACCCATCAAAGTGGCAAAACATGAAAAAAAGCTCATCATCA
 CTGGTCATTAGAGAAATGCAAATTGAAACACATGAGATAACCATCTCAT
 GCCAGTTAGAATGGCGATTATTAAAAAGTCAGGAAACACAGATGCTGGA
 GAGGATGTGGAGAAATAGGAATGCTTTACACTGTTGGTGGAGTGTCA
 TTAGTTCAACCATTGGGAAGACAGTGTGGCAATTCTCAAGGATCTGGA
 ACCAGAAATACCATTGACCCAGCAATCCATTACTGGGTATATACCTAA
 AGGATTAGAAATCATTCTATTGTAAGACACATGCACATGTATGTTATT
 GCAGCACTATTACAATAGCAAAGACTTGGGACCAACCCCTAATGCCACC
 AATGATAGACTGTGAAAAATGTGGACGTATACCCATGGAATACTAT
 GCAGCCATAAAAAGAATGAGTCATTCTTGCACGGAACTGGATGAAG
 CTGGAAAGCCATCTCAGCAAACACTAACAGGAACAGAAAACCAAACA
 CTGCATGTTCTCACTCATAAGTGGGAGTTGAACAATGAGAACACATGGAC
 ACAGGGAGGGAAATGTACACACCAGGGCTGTCAGGAGGTGGGGGCAA
 GGGGAGGGATAACATTAGGAAAATACCTAATATAGATGACGGGTTAATG
 GGTGCAGCAAACCCACATGGCACATGTACACCTACGTAATAACCTCCAT
 GTTCTTCACATGTATCCCAGAACGTAAGAAAATTAAAAAGAAAGAA
 AGAAAGAAAAGGATGTTACGACAAACCAAGAAAGTCAAGCATGTCATGA
 ATAGTCGTGTAAGTCACAATAAGAGGATTATTTAAAAAAACTTTTATA
 TGATAAAAGTTGCTATAATTAAAGGGAAATTATAATGGTCTTCTAGAGA
 TTGGGTTGATGTTAAAAAAACTACTTATATATTAAAAAATTGGTTAGAAC
 ATGAAATTCTTACGGGGTTGATTCACTCTTAATAAAATTATAAGAGACT
 TAAGAATTCTCTCCCTTAAACCCAAAGTCACTTATTGCACTTGTGCTGTT
 TTAGGTTCTCTCCCTTAAAGGGTGGGAAATAGTAATGCCCTCCTT
 CAACTCCCTCAGCTCATACGTTTACCCCTCAGATTCTGTTGTTG
 TGTCCCTGATGCTAACATGTTCTTAAAGGTCTAAAGGAAATGTTTCT

FIG. 3 (14 of 52)

TCCAAACATAATATTCTG1GCATTGAGAAGGTCTTTCTTTCGCTTTG
 GTAACTGGCTTAACAGATTTATGTTTATTGAAATAATTCTATGCCAT
 TATTATTAAGTTTGGTTGCTTAGAAAACACTGAGATTAATACAATTT
 TTAAAAATTATGATTATTACATCCATATCTTATGTATGTGCTTTAA
 AGTCCTTGTGACATTGAGTTCTAGGGCTTGACTCCTGGGCTTAAAGGA
 CAAGTCCTGCTAACTTAAATACTGACAGCAATTAAAGGCTCATCTCA
 GGACTGGTAGAAAATGCCATCAAATAACTGCATTCTGAAACACAGA
 GCCAGAAATTAAAGCTATTCAACTCAAGGCCAGGAACATAGTGGAAAGA
 GGTGGGTGTGAGATTGTAAGGGCCAATTGGAGAGATAAAATAAGTTC
 AATTCTCTATAAATTACATAATCATTGATGTCCAAGGCCACACTGATG
 CAAGATCAGCATAATGGGTCTGTGTCAGATTAACAAGGTTTCTTGAAGC
 ATTAACCTACTCCTTAATAAAGGTTAGAGGTTATAAAAGGCTCTGGA
 AGTTATAGCTATGGTCAAGATAAAATTCTAGATTGTTAATACAATT
 TGGAAAACAATTAAATTGGCTTCTGCTGTTTATTAGGGCTTATTGT
 TTGGAAAATTAAAGTCTCGTCTCAAAGAACATGAAGGCTTCACCTTTT
 TTTTTTTTTTAATCCTGAGTTACACTTGGTCAAATGAATGACTTA
 TTTTACAATGACCTTCATCAAGTGTAAACCTTCAAATTGACAAA
 CTTTCCAAAATCAAACATAAAATTATGCTTTTATGACCTAATGAATCC
 TTTAAAATACTAGGTTCCCTAAAGTCCAAAAAAATAACATAA
 TGTGGCTTATTGGTATAAAATTACAAGAACATTGTCAAATATAAA
 ATATTGGTGTGGTTTGGCTGTATTGTATAAAATATGTTATTGGTA
 TGTGTCCAAAATTAGGAAACTCCTATAATTCTGATATGACTTGGTGT
 ACATTATCAGTAATAATTATAATTGTTATGGTAAATTATTGTGTGCCATG
 GAGGTAACAAATTTCCTCATCAAGTGTGCTTGAATGGTGGCCCTAA
 AACCTTTGCCATTCACAGACAATTGCTTGGCTTGGCCCTTTAGAAG
 GTGGTTTATAATCAGCTATAAAACTCTAACGGGTGCTTGAATGCAGG
 CTTAAGATAGCTTGGAGACTGTGACATCAGAACAGAGGAAACTTCA
 GTATTCAATGGAGTGCTGAAATATTCAATGAAATATCAAGCAAAACAGGAATT
 AACATCATAGATGGAACCTAAAGAACATGCTGAAGTAATCTTTGACTTT
 TTTCTTAGAATGTTGATCTCGTTTGTGTTTCAAGAGTCNAGGAAATT
 TTCTGTTGAGATATTGACAGCTTAACAATTAGTATACTCCAGTGAACA
 CAATTGGAGCA

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ATCTAGTCATCCCCAGCCTGACCAATTCAATGGCCCCATCTAGTTAA
 AATTCCCTACCCCTGACAAGGCCCATCTACGCCCTGACCTCATGCCCTC
 CACTCTCAGTCTGCACTCACCTGCCACACTCAAGGGCTTCCCAGGTT
 CCTTCTTAGATTCCACCGATAGCTCAGGGACTTGCACATGCTACGGTCT
 CTGCCCTGGCTCTCCCCAGATCTCTCATGCTTAGCTGCTTCTCATCAGC
 ACCCTCAGAGACTGTCCCTGCCAACCTCTCAGGTTCCATACCTGCCA
 CCCTCCCCAATCAGTAACAGTTCTCACAGAGCGAGTTACCATCCCA
 GTATTCCCTAACTTATTGGTACTGGTCTGTTGCCGTGCTCCACCA
 CAAGAACATAAGCTGCATGTGAACAGGAGCCTGTCTATCTGTCAACCC
 AGTGGCTGTGACATAACCTGATACACATTAGATGCTCAATGATGTTGAT
 GAATGAAGTGTGGTAGTCCAACGTGTTCTTGTCTGTGTAAGTATGT
 CTGTTGTGGTTCTAAGAACCTACAGCTCTCCACTGTGACTCTGTTC
 TATGGTCTGATTTGCTGGACTAGAACCTAACCCTACATGCTTACTCTTA
 GTGTCCTCCCCAGAGGGCTGAATCCCAGTCCCTAAACCTCCACCAAATGG
 CTAAGACCTAGCTTCAACCAGACAGGCCACGGCTACGCTGAGACCTCAGCACCG
 CCCTCTGCCGTCTCATCTTAACGCATCCTCAGGGCCAGCTAAATG
 TCTCTCTTCAAGGAAGGCTATCTCTTCTGCCCTCAGTGTCTCCAT
 GCCTCTCTATGCCCTCATGCCCTGTTCAACCCCTGAGAACAGTGGAGAAA
 TTGCTAATCTGCTGTGTTGACACTGTGCTGGGGTGCCTTGGCCAGGGAG
 CAGGCTGGTGGTGTGCTGATAGCCCGTGGCTGCCCCAGGTCCATGCTCA
 CTTCTGAGCCCCAGTGGAGTAGGGCTCCCTTCTCCCTATTGCGACACTCA
 GAGGAAGGACGTGCTTCTAGGACAGATCTGGCCAACCTCTCCCTCGTGA
 GAGAACAGGCCAGCCATCTCTGCCCTCTTCTCTCTGCCCTGGAGT
 AATAAAGGTGCTGGTCAAGAGCCTCTAGAAGGAGACCCAAACATCCACC
 ACACATTCCCAAGTCCAACCGTCACTCCACATGGCTGGCTGTGCAAGGTAAA
 CGCAGAGTGTGTTACACACCCAAACCATCTAGTATTGGATGGGAGGACA
 GTAGCGTGAACACTCTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCA

ACCCAGATACCAGAGGAGCCCTGTACTGGGATGCTATTGGATGGTTG
 AGTCATGTACAAAGTTAGCCCTTGTATATAGAGTTAGCTACGTACATC
 TTCTCTGTAGGGAACCAAGAGGGAGAAGAGATATGTAGTAGGATT
 ACCTGCAAATCTCTGTGAGCACCCCTGCACTACATACAGTGGTAGCAT
 GTGGTAGGTGCTCAATAACTATTGACCGATAGATTGAATACAGGTAGGAT
 GGTGACACAATCTAAGATCCCAGGGTGGGAGACCACACGCTGGTTAG
 GGAGACCAAAGTGGACCGTGTGGCCAGAAGAGTCCCCACTGCACTCTA
 GTGACAGTGCAGAAAGTCACTGTGGAAATCTAGAAAGTTCTACAGGTTG
 CTATTCATCATAGCACTGTGCAGGCCAACCCCTGCTCCACTGGCTG
 TTGGAAAAGCTTCTTTCTAGCCAGGGAGCTCTCAAAGTGT
 CCACCTCTCACCTCACCCAGGCCTCAGGTGTGGAGGACACTGCCGG
 CTGCTTGTCTGCTGACTCATCCCTGGTTCACTGGAAAACCTACCA
 AGCTGGCCTTTCCAAGCATCAGCCTCTCATTTCTTAATCCCTTAGG
 TGTGATCTCACCTCACAGTAGATTGCCTCAAGGCCAATCCAATAT
 GAATAAAAATGATTATTTGTATCTCCAATCTCCTTTAAAATATTA
 TTTATAATCCCTTAGGAGGATCACCTAAGTGAAGACTATTTTACCT
 AAGAAATGTTAAAATGTAAGACATGGTTGTAATCTGGGGATCCTGTTA
 AAATGGCTAGCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAG
 TGGTTGCCTTGAAGGGCGAGTTGTAATGATTTCTCCATTTC
 TGCTTCCAATTCTACAAAGGCCCTAATATTACTTCGATAACCAGGAC
 CTCTGATAACCTGCCCTCACCGAGTAAAGACTTAGCTGGAAAGTCAGCT
 TCATGTGAGGTAAAAGGAACCAGGTAAATACACAATTCCACTGCCA
 TCGGGTGTGCAGGCCTGAGCTCCTGCATGTGGAGGAAAGAGAAAG
 AGAGAAACTCCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGG
 ACGCAGAAAGCTGAATGGCACAGTTACACTATTGTGCTGAGGTTCTG
 GCCTCTGGCTCTTGACAACCTGGCAAAGACCCACAGAAA
 ACTATCT
 AGACCCCTACCTGTGGGAGGGAAAGTGTCTAACATCT
 CACCTGGACCTCAAATGGCTTACAGTTCTCATCCAGGGCTTCA
 TAGTACATACCAGGTGCTAACGCTGGGTGCTGGAGACATGACGGGAACCC
 ATTACCATGGCTTGTACTGTGACATTACATCTAGGGAAAGCCAGCA
 AAGGGGAGGGATCGAGGAGAGCTTGTAGGAGAGAAA
 ATACCAAGGGC
 AAGGGAGAAGCCAGCCTGTTCTGAGCACACACAGTGGTCCATCTA
 ACTGGCCTCAGTGCAGGGTGGACTGGAGATGGGCTGAGGAGCTGT
 CACAGA
 GCATTCTGGACACAGATGTACATAGTCCCTGAGGTTAGGGCTT
 TAGG
 CATGGCAGCATTGCTTGTAGTTCTTGTAAATGTTGCCATT
 CATGA
 CAATGTGGAAGATGGGCTTGAGAGAAGGGCAGGGCTGT
 GAGACCAGT
 TAGGAGACTAACATGTGAGCCAAGGAAAATGAGGAACAC
 CTGAAACACTGG
 GGCAGGTGCAGGGCCCAGAGAGAAGCAGATGGCTTCTGAGGTT
 TAAGT
 AGGTAGAATCAAGGCAGCTGGTACAGATCTTTATTACATATA
 AACACTGG
 ATAAGCCATCTGTTCCAAGACAAAAGAGTAGGCGAAA
 ACAATACAAGAC
 AGAAATGGAATTAGAACAAACCTGGAGGAATGTGAAATTAGAGTAGAGA
 GTCCAACACTGGCTGCAATCATAAAAATGTA
 AAAACAAA
 ATTTGCT
 AGGTGTGCTTACATTAGAAATAATTAGCTGT
 CATATTAAAGTTCACTTGT
 TATGGCTTAAATGTGTC
 CCCCTTAAATGTGATGTGTTGGAAACTTGT
 GATCCC
 CAATGCAACAGAGTTGAGAGATGGACCTTAAAGGTGATTAGGT
 CATA
 AGGGTTCTGCCCTCAT
 AAATGAATTAAATCTGTT
 ATCATGAGAGTAGATT
 CCTGATAAAAGGATGATCTCTGCTCCTCCCCACAGCCCT
 CTGCTG
 CTTCTGCTTCCACCTCTGCTATGGGATGACACAGCAAGAAGGCC
 TCACCAATGCAGCTCTTGATCTGGACTTCCAGCCT
 CAAACTGTA
 AGCCAAACAAATTTCTGTT
 ATTATAAATTACCG
 ACTCTCAGGTATTCTG
 TTCTAGAAACACAAAATGGACTAACAGAT
 CATTAAATTATCATT
 TTTTATCA
 GACTGTTGA

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AAAATATAACAGAGAGTAAGAGGAAAATTACCTTCTTCTTTCTT
 CCTGCTGACCTTATTCA
 CCTCCATCCCAGAGCATCCATT
 GATCTTACTGACATCTATTATCTGACCTACACA
 ATACTAGAGACATTAGGA
 CAATGTGGCTGCTCCAAGAAACTCAA
 ATAAGCCA
 ACTGAGATCAGAGA
 GGATTAATCAC
 CTGCCAATGGG
 ACACAAAGCA
 ACAAGCAGCTGGGAGGCC
 AGTC
 CCAAAATGGG
 CCTGCTGCTTCCAGT
 TTCCCTCTCTGCA
 ATTGATGTCA
 GCATTATC
 CCTCGTCCCAGTC
 CCTGCTCCACT
 ACCACTT
 CCCCTCAAA

FIG. 3 (16 of 52)

18/118

CACACACACACACAACAGCTTAGATGTTTCTCCACTGATAAGTAGGTG
 ACTCAATTGTAAGTATAATCCAAGACCTCTATTCCAAGTAGAATT
 TATGTGCCTGCCTGTGCTTTCTACCTGGATCAAGTGATGTCTACAGAGT
 AGGGCAGTAGCTCATTGAACTCATTCAACAAGCATTATTCACTGAG
 AGCCTGTATTTTCAGGCATAGTGCCAACAGCAGTGTGGACAGTGGTGC
 ATCAAAGCCTCTAGTCTCATAGAACCTAGTCTCTGGAGGGATATGGAAAA
 CAGACAACCCAAACAACCAACAAAAGAGCAAGATGCTGCAAAAAAAAA
 AAATGAATAGGGTCTAAGATAGAGAAAAGTGGAGAGTGCTATTAGAC
 AAAGTGGTAAAACAAAGCCCCCTGTGAGATGAGAGCTGCCACAGGAGG
 GGGCGGGTATGGTTGTGGGTTTGGGTAGGACATTCAAGAGGGGGGC
 GGGTCTGGTTGTGGGTTTGGGTAGGACATTCAAGAGGGGGCGGGT
 CGTGGTTGTGGGTTTGGGTAGGACATTCAAGAGGGGGCGGGT
 GTTGTGGGTTTGGGACATTCAAAGAGTCTGAATGCAACCCAGGCCTAC
 AACTCAAGATGGTAAAGGACAGCTCAAGGATCAGAAGAACATGCTTG
 GAACCTGGGCATTTGAGAAGGAGGAAAATATGCAGAGACTAGTGCTTG
 CAGAGCTTGCATGTGGATTCAATTGAGGTACAATGAAAACCTTAATG
 GGTTTCAACACAGTCAATGGCCTGACCTCACTTATATTCTAAAATAGA
 AAACAGATCAGAAGGAAGGCAATAGAGAACAGAAAAGTCCAATGAGGAGG
 TTTCACAGCAGTCATGGGGTGGGTAAGGAAAAGAACAGTGGAAAGAAC
 GACAGAATTGGTTATATTGGAGATAGAACCAACAGAAGGAAGGAGGAG
 AAACAAACATTACTGAGAAGGAAAAGTAGGAGAGGAATAGTTGGGA
 AATAAAATCCTGTCGACATTGAAACCCCAAGGAAGCCTCAAAAGTATATT
 TACTTGCTTAGTTAAAGAATAGGAAAGAACATCTCAACTTGGAAAT
 TTGAAATCTATTTCATAAAAGTATTGTTAAATTCTACTCATACTCAC
 AAGAAAAGTACATTCAAAGAGTATATTGAAAGAGTTACTGATAACTT
 AGGAATTGGTGTATGTTGTTGTTGATGCGTGTGTTAAC
 CTTCAATTGTTGACTTAAATACTGAGATAATGTCATCTAAATGCTAAAT
 TGATTCCCAAAGGTATGATTGTTCACTTGGAGATCAAATGTTAGGG
 GGCTTAGAATCACTGAGTCTCAGATTGATGCAAAATGCTTAGGCCT
 ATGTTGAAGGCAGGACAGAAACAATGTTCCCTCACCTGCCCTGGATAC
 AGTAAGATACTAGTGTCACTGACAATCTTCATAACTAAATTGATCTC
 TCCAACTCAACTAAGGAAATCAACTCTTATTAAATAGACTGGGCCACACATC
 TACTAGGCATGTAATAATGCTGTCGAAATGAAACAAATGAATGAAGAGCC
 TATAGCATCATGTTACAGCCATAGTCTAAAGTGTGTTCTCATGAGG
 CCAAATGCTAAGGGATTGAGCTCAGTCTTTCTAACATCTGTTCTC
 TAACAGAATTCTCTTCTTCATAGGAGATGCTGAGATACCCAAA
 CCATCACAGTAGTGTGACAGTTCATGTCATGACTGAAGAACGCTAA
 ACTAAGAACATTTCACATCAGTTGCCCATCCTAAACTTGTGTTATGCCAC
 AAAGCAAGACTACTGGGTGTGCTGGCAGGGGGCCACCCCTATCACTG
 ACTTTCAGATACTGGAAAACCAGGGCTAGGTCTGGAGTCTACTGTC
 ACTTGTGCACTGTTGACAGTTCATGTCATGACTGAAGAACGCTAA
 ATCCTTACTGTTAGTCATTGCTGAGCATGANTGAGCCTTGTAAATTCT
 AAATGAATGTTACACTCTTGTAAAGAGTGGAAACCAACACTAACATATAA
 TGTTGTTATTTAAAGAACACCCCTATATTGTCATAGTACCAATCATTTA
 ATTATTATTCTCATACAAATTAGGAGGACCAAGAGCTACTGACTATGG
 CTACCAAAAGACTCTACCCATATTACAGATGGGAAATTAGGCATAAG
 AAAACTAAGAAATATGCACAATAGCAGTTGAAACAAAGAACAGCCT
 AGGATTTCATGATTCAACTGTTGCCTCTACTTTAAGTTGCT
 GATGAACCTTAATCAAATAGCATAAGTTCTGGGACCTCAGTTTATCA
 TTTCAAAATGGAGGGAATAATACCTAAGCCTCTGCCGCAACAGTTT
 TTATGCTAATCAGGGAGGTCTTTGGTAAATTAACCTCTTGAAGCCGAGC
 CTCAAGATGAAGGCAAAGCACGAAATGTTATTAAATTATTATTTA
 TATGTTATTTAAATATAATTAAAGATAATTATAATATACTATATTATGG
 GAACCCCTTCATCCTCTGAGTGTGACCAGGCATCCTCCACAATAGCAGAC
 AGTGTGTTCTGGGATAAGTAAGTTGATTCAATTACAGGGCATTG
 GTCCAAGTTGCTTATCCCATAGCCAGGAAACTCTGCACTTAGTACTT
 GGGAGACCTGTAATCATATAAAATGTACATTAAATTACCTTGAGCCAGT
 AATTGGTCCGATCTTGACTCTTGCCTAAACTACCTGGGATTCT
 TGTTCAATTCAATTCCACCTGCAATCAAGTCTACAAGCTAAAATTAGAT
 GAACTCAACTTGTACACCATGAGACCAGTGTATCAAAACTTCTTTC

FIG. 3 (17 of 52)

19/118

TGGAAATGTAATCAATG1 . CCTTCTAGGTTCTAAAATTGTGATCAGACLA
 TAATGTTACATTATTATCAACAATAGTATTGATAGAGTGTATCAGTC
 TAACATAAAAGCTTGAACAAATTCTCTGACACATAGTTATTGATTG
 CCTTAATCATTATTTACTGCATGTAATTAGGGACAAATGGTAAATGTT
 TACATAAAATAATTGTATTAGTGTACTTTATAAAATCAAACCAAGATT
 TATATTTTTCTCCTTTGTTAGCTGCCAGTATGCATAAATGGCATT
 AGAATGATAATATTCGGGTTCACTTAAAGCTCACATTACACATACACA
 AAACATGTGTTCCCACCTTTATACAAACTCACACATACAGAGCTACATTA
 AAAACAACTAATAGGCCAGGCACGGTGGCTCAGACCTGTAATCCAGCAC
 TTTGGGAGGCCAAGGTGGGAAGATCACTTGAGGTCAAGGAGG
 GCCTAGGCAACATAGTGAGATCTCATCTCACAAAAAAATGAAAAAT
 TAAAAAAATGAGCTGGACATGGTAGTACACACCTGAGTCCCAGCTACTCG
 GGAGGCTTGAGGTGGGAGGATCACTTGAGCCTGGGAGATGGAGGCTGCAG
 TGAGCCATAATCACACCATTGCACCCCAACCTGGCAACAGAGTGAGACC
 CAGTCTAAAAGATAAAATTTTAAAAATGTTAAAAAAATATATAAAAGAGA
 ATTTAAAAGAACAACTAATAGATCAAAGCATGGATGCAAGATATTTA
 GTTGGAAAATCAAGGTTAAAATCAAGGGATTTGGAATTAGGTGTGGTAG
 ATTTGGGTAAGGAGTAGTCTAAGATGACCTGTTCTGGTAGGAGAC
 TGGATGAGTGGCAGCGCTTAACCATATTTGGTAGAAATATGGAGGTC
 TTCTCCATTCCAGGATGAATGATGAGTAAATTTAGGCATGTAATTGAG
 GCTACTAGAAGGACACTCAATTGCAGATGTAATGGGAGATGATAACC
 TATCTGGAACTCAGAAAAATAACTGTATATAGATATGAAAGACATCAGTA
 GGTATGTTAGATAAAATCCTAAAGTGTCAAAGGGAGAAGAGAAG
 TATATGGTGAACACTGTTGTTGTCATGCAATTGCCATCTCTTCTT
 CCTTACTGACAGAACCCCTGATTCACTGAGAACTCAACATGCCCTCCCC
 AATTGATGAATCCAATTGGTTGAAGATTATGTCATTCTATTCTACATG
 ACTAAGTCACGTTGACTTAATCCTATCAAATGAGATGTCATCTGAAAC
 AACTCTGAAAAGATTCTACCTTGATAAAAATAAGAGCCATATAGAT
 GGTCTTTATCTCCTTCTCCTGAAATGAGATATGTCATGAGGAAGT
 GAAGCTTAGAAGACTGTTGTCAGCAACTTGCAACGACTGGGAAGTCAGAGCC
 ACACAAATGAAGAACATGAGTGGAGGAGAAAAGAGCCAGCATCTGAA
 CAACATTGTTACACCGAGAACCTACCTCCAGATTAAAGAAAACAAGAAA
 TGCTACTGTTATTAGCATTTCACTGGGTTGCTATGACTTGAGTCAA
 ATCTAGCTTAACGATACAGAGCACACAGAGAACTGGCTCTCATTTGT
 CTCATCCTGTTCTCTAGCAGCCACGACTTCTCTAGGGTTCTTAGCC
 CAAGCTGGCTAGAGCAAGACTAAGACTTGATTCTTAATGTCCTT
 TTGTTTAAGAAAATTAAAGAATTATTTTATAATTATATTTAAGA
 AATAAGGAAATACAAAACACTGAGCAAGCAACACAAATTCAAGAAATCTT
 AAAAGTATAATAGCTGCTCAGTCTGTGATTAACAGTGAATATGGAATC
 ATTGTTAGAAATGGCCTGGAGCGTTATTCTCCAGGCCAGCTATCTTAT
 GGTCTGCCCCACCTCCCTCATGGCTAAACAGTAAGAGAGTCCCATGGTG
 AGACTCAACAGTCTTAGCACAGAACTTGTACAGTCTATTCTTTCTTA
 CAGTCCATATATCAATTCAAATCAATGAGAGTAAAGCCCAATCCCTGC
 CTTTAAACCCAAAGGACAGAACGCCCCAAGGATATTCCCTAACCT
 TCTCCCCCT
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CCTGTCGCTCCTATGTTAAAGCTGGGATCTCTTTCTGTGCTAA
 TTATTTCTCCTATTGGCTTGAAAATCTGATAAAACATTAGGACTGTG
 TATAAAATAGAATTAGCAGTCATGCTTTATTGAGAAATTCTCA
 TGGACGTTGCTACTCTCTGGCTTCTGGCTTCTCATGGCTTCTCAGAT
 CCCACAGTAAGCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAA
 TAAATGAAGTGACTTTAACCTACTGATATGGCTTAAAGAAAAGGAGTGG
 CCTTTAAGATCCATGAACTCTCAAACAAAGTGTAAACGTTATCTCCAT
 GCATATATAACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAA
 GAAAGGAGACCCAAGTGCACATGAGTATTGCCAGATTCTCTGTGTTCA
 TCCCACCGAGGAAACAAAGCATGAGTATTGCCAGATTCTCTGTGTTCA
 AGAAAAGCCAGAAATCCAGGTTTGCCTGAAATGTCCTGATTAAATGT
 TGGGAACTAATTATATTGAAATAACATTGTGTGGGACAAGTGAACCT
 GTATGTGGAACTGCTTCTCCAGTGGCACCAGTTGGACCCTGATAC
 TCAGCAAGTTAGCAGGCCAAAGTGCCTGTCATTGTCAGTCATCAAGGTGAT

FIG. 3 (18 of 52)

20/11/8

GTGTGATTGGTCAAACAATTAGTTTGCTCAGCATCTCGTGTGTTTCAA
 AGGACCTGAGGGTCATTTGCCATGCAGATCTTGTAGTCCTGTTTATT
 TATTAATTATCTTGCAGAACATCTATAATGTTTATTTAAGCAGCGAGAGC
 CGTGGCAGCCTTGGCTGGACCCCTTCTAATGATCATTAGTATCAGGC
 TATGTGGAGGTGATTGTTGCAATTGCTGAAAGCCAACAGTATCACTC
 CTCCCTAGGGTGGCAGAGATGTGAGAGAGGGAGACTGACAGTCTGTGG
 GTGTGTTATGCACTGTTGGGGAAAGCAGGGCACAGGGACAATACTGTGG
 GTATAAAACTAGTCTAAGGTAGCATCAGGAAGTTCATGAAGCCAATGAA
 TTTTATAACAGCACAAGACATTATTTGTTTGCCTCCCTCTCATTTT
 TTTTTTTTGAGACAGAGCTTGCTCTGTCATCCATGCTGTGCAGT
 GGTGCAATCTCGGCTCACTGCAACCTCCACCTCAGGGTCAAGCAATT
 TCATGCCTCAGCCTCTGAGTAGCTGATTACAGGTCTGACCACCCGCC
 GGCTAGTTTTGTATTTTAGTAGAGATGGGGTTTGTAAATGTTGCCAG
 GCTGCCCTGTCACTTTTTACTAGTGTCCAGTGGAGTTTTAGGG
 CTACATAACATGATACTGTCTTAATCTAATGGCTAATGAAAGGGATATG
 TATATGTTTTGTGTTAAAACAAACTCTTGGGTCCTCAATAATTT
 TAAGAGTATAAAGGGTCTGAGATCAAAGAGTTGAGTTCTGCTGGACT
 GGGACAGTGGTTGTCAACCCAGATTGTACATTAGGGCATCTGGGAAGCT
 TTAAATAGTACTGATGCCAACCTTACCGCAAACCAATTAGCCAGAAT
 CTCTGTGGATGAGAAGTCTCATTGTCATCATCACCAGTACCATCAT
 TGTACCCGTCACTACACCATATCATCATCATCATCATCTTCATTATC
 ATTGTTAGTATCTCCATCACCACATCAGCATCACCATTATTATCATCAT
 CATCATCCCCACCATCATCCTCATCGGAACCTCACCTGCATGGAGGACAA
 TCCACTATGCACTAGGTCTATGCTATTGCTATACTCCTTATTCTCACA
 ACTGCCAGAGAGGCTGATATTCTCACTTATAACAGGAGGAATCTGG
 ATCGGAAAAGTTAAGGTAAAGCTAATTCAACAGAGCAGAGAGATAGAGCC
 AGGATTCGAAACCAAGTTCTGTGCTACATCAATGTTCCAGTCCTGCAC
 ATTGAGAACCTCTTAGTTATGCTTCAACCCCTCCAACACCAACAGTAAAT
 TTTTCTTTTAAAAAAATTATACTTTAGTTATAGGGTATATGTGCA
 TAATGTGAGGTTGTTACATATGTATACATGTGCCATGTTGGTGTGCTG
 CACTCATTAACTCGTCATTACATTAGGTATCTCTAATGCTATCCCT
 CCCCCTCTCCCCACCCATGACAGGCCCTGGTGTGATGTTCCCCACC
 CTGTGTCCAAGTGTCTCATGTTCAAGTCCCACCTATGAGTGAGAACAT
 GTGGTGTGTTGGTTCTGTCTGTGATAGTTGCTCAGAATGATGGTT
 CCAGCTTATCCACGTCCCTACAAAGGATATGAACTCATCCTTTTATG
 GCTGCATAGTATTCCATGGGTATGTGTGCCACATTCTTAATCCAGTC
 TATCATGGACATTGGGTTCCAAGTCTTGCTATTGTGAATA
 GTGCACAGTGAACATTCACTGTGCATGTGCTTTATAGCAGCATGATT
 TAATCTTTGGGTATATAACCCAGTAATGGGATGGCTGGTCAAATGGTAT
 TTCTAGTTCTAGATCCTGAGGAATTGCCACACTGTCTACCACAATGGTT
 GAATTAGTTATAGCCCACCAACAGTGTAAAAGCATTCTATTCTCCA
 CATCTCTCCACGACCTGTTGTTGACTTTTAGTGTGATTGCCATTCT
 AACTGGCACACAGTAAATTATAGATTATAAGCAAATTGTATT
 CTGTGCAAGAATTGGTTATTAAACCATGTGTTGCAAACACATAACAT
 GGTAAATTGTGATATTGCTCAGTACAAGATCATCAGATCACTACACAGA
 CTTGAGGTAAATTCCACCTAAAGCAAAGAGAACTGACCCACATTAACTG
 AGAAGTCTTACTTATTCTACCTCTAATGACGACAAATGAAAGAGAAG
 GCCTTAATGTGGTTAACTATGTAATTCTGACTTTGAAATACTG
 AGAAGAGCTCATGACTCTCCATCTCTAATTCTACCTGGTGGATT
 GACTGACCACAACATGGTAAATGAGGGAAAGCAGAATAAGAAACCTTG
 CTTTTTTCTCTCTGTTGGCTGGCTGAGTGGCTCACACCTGTAA
 TCTCATCACTTGGGAGGCCAAGGTGGGAAGATCACTTGAGCTCAGGATT
 TCAAAACTGGCTGGCAACATAGTGAGACCCATCTCTAAAAAAAAAAA
 AAAAAAAAGGCAGAGCGACAGGCCGTGCGTGCCTGTAATCCTACCTACTC
 AAGAAGCCGAGGTGAAAGATCACTTGAGCATGGGAGGTCAAAGCTGCAG
 TGAACTTGATTGCACTTCACTCAGCCTGGGTGACAAAGCAGGACG
 CTGCCTCAAGAAAACAAAACCTTAATTGGCTATTCTTTC
 TGGTAAGAATGGTATAGAGATGGGGATGAGGATGGCTATTGTATGAGAGA
 GCAAACAGGGTCCAAGCAGTGTCTGGCTGTCTAAGGACCAGTAGTCAG
 CTTAACCTCTAAATTCCAGGGAAAGGAGTCGGAGTGGTAGAATATCCT

GGGTATGCCAAAGCATACCTGCAAATAGCCTGTCATGAATAATTG
 TTCATTTGTTATGACTGGAAACTGGCTTGTATGCCAGAGAATGGGG
 CAGGAAAGAGAGATTGGTGCTTGAGCTCTGTGCCTCTGGGGCAGTGA
 TGCTTTCCCTCATGTGAAGGAGAGCATGACTGAAAAGGTGCACAAAT
 AAGGTGCTGTGAGAGAAATTAAACCTTCCAGATAACAGAGACACAACCTC
 CCCAAGAGGTCTCATTGCTCTGCCCTTTCTTTCTTTGCTGTTCT
 ACCATTAATAACAGAAACTGATTATGACCTCAAAAGAGAGGAGAAAGCGA
 CTCTCCCCACCCTAGAGCTAGTTAACACCATACTTCCTAGATATCCTT
 GAGAGCAATGTAACCC

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GTGAACTCGTTTACCTGTTAGCAGACCAAGCCGAGACAAAATCCNTC
 AGACACCAAATTAAAGAAGGAAGGGCTTATTGGGCCTGGAGCTGCGGCA
 AGACTCACGTCTCCAACAACCGAGCTCCCAGTGTGCAATTCTGTCCC
 TTTAAGGGCTACAACCTAAGCGGTCCACATGAGAGAGTCGTGATAG
 ATTGAGCAAGCAGGGGTATGTGACTGGGGCTGCATGCACCTGTAGTTA
 GAATGGAACAGAACATGACAGGGATCTTACAGTGTCTTCTTATGCAAA
 TAACCGATTAGATCAGGGTCGATCTTACCAAGGCCAGGGTGTGTCACC
 GGGCTGTCGCTTGTGGATTCTGCCTTTAGTTATTACTCTTT
 CTTGGAGGAGAAATTGGGCATAAGACAATATGAGGGGTGGTCTCCTCT
 CTTACCTGCAGGGAGTGTGAGCTAAACTCCTTAAAGGAGTTACCTGCCTTC
 CATCATCAGGGAAAGCAGGAAATCTGCCTTCTTGTGGAAGCAAGTAAA
 ACTCAAAACAAACAAAGAAAAAAACAGGGAGTTGTACAGCAAATAAACT
 TTTGATTTGACCAAATTGGGAGATCAGGAATTCTCTGAAGGAGATGC
 TTTCAGACCTCAGCAAATTGTCCTGTGGTTGAGCCATAAGTAGCTC
 ATGCTGGTACCAAAACACCACTAGGAGATTGTCAAAGGTAAGAGGCATCT
 CCACTCAGAACTCCCTCGGTTACCAACATGTGAACCTTGGAAATCTGA
 GACAGGTCTCAGTTAATTAGAAAGTTATTGCCCCACGGTTGAGGACAC
 CCACCCATGACAGAGCATCAGGAGGTCTGACCACATGTGCTCAGGGTGG
 TCTGAGCACAGCTGGTTTACACATTAGGGAGACATGAGACATCAGT
 GAATATATGTAAGATGTACACTGGTCCCTCAGAAAGGCAGAACAACTT
 GAAGCAGGGAGGGAGCTTCCAGGTACAGGTAGGTGAGAGACAAACAATT
 GCATTCTCTGAGTGTGATTAGCCTTCCAAGGAGGCAATCAGATAT
 GCATTATCACAGTGGAGGAGGGTGAATTGAATAGAATGGGAGGCAG
 GTTGCCTAAGCAGTCCCTAGCTGACTTTCCCTTAGCTTAGTGTGATT
 TGGAGGCCCAAGATTATTTCCCTACATCACTGTGGCAGCTGACT
 AGGAAAGCTTGTAGGACTGGTGGCAGTGTGAGAGGCCAGTGGGGGTG
 GTGGCTGTGCCAATGGTAGCAACCACCTGTGAGGCTGAGTAACACTCAT
 TTCCCAACCTCCTCTAGCAGCCCCAGTGGAGATACAGAGGAAGCAGACTA
 GCGATACAACCCAGCCTGAAGTTGTCTGGTAGTGTAAATGGAATAAAA
 ATGGGAAGGGTGTGAAGAGACCAAGAAAATGGTAGAAGAGATGGGG
 CACAGAAAATTAGCTGGATCAAAAGGACGGAAAAGCAGAAAGGCCGAT
 AGAGAGAGGGGATATCTATGGGTCGCATTGTAAAAGGACAATCACT
 GGTGCTTGTGAGAGAGAGGGTAGAAAGCAGGAAGGCTGGAGGCTGTC
 ATCCAAGAGGGCGACATCTGTGAACATGATTCCAAGAGTCACAGACCAT
 GGGGGTGGCCAAAGGGAGTGCCTTCTCACCTCTACTCTTAATTCTT
 GTACTCAAGATAATAAGTCCCAGAAGAGAAGTACCCATATTAAATTCT
 CTGTGCTTCTCTAGCAGTACTAAAAATATTATGAAAGGTATCAAACCT
 TTGAGAATGTGTGCTGCTAAATTGTTAAGGATGCTGGAAAAGCTAACAGC
 TCCCTGATCCTGAGCTGAGTATGAGCCTGTGGTAGGCCAATGCAGGTC
 TCCATTAGACAAAGGCCAGGGACGGATGAGACCTAGGGACAGAGAT
 GCATGCTGGAGCAGCATCCCCACTCCACTGCGACTCAGGCCAGCTGAC
 TGCTTATGAGTAAACGTTACAGGGAACACTTGCAGTCTTAACACACA
 TGCCCCACCTGAGCAGCAATGAGACAAAGCTATCCTCATTAGGAAGGAAAGGAA
 GGAGGAGGGAGGGAGGGCAAACGAATCTTCTGCTTGTCAACCACGTCCA
 TCTCTGTTAGGTGATTTCCATGTGTGACTTTGTTATCTTATAATAAC
 TCTGAGAGGTAGGTCTGATGTCCACATTGAAACATGAGGGACATCCAGC
 CAGGAAGTTGAGTTCTGGGACATAGCTGAGAGGGCAAAGCTACATATAA
 ACCCCTTTGTTTCTGGCTTATCCACTGAGTGTGCCCCCTGCAATCCA
 CCAGCCCATTGTGAAGTGCATACTATAGGTAAAGTTGGCACAGGGAGT

FIG. 3 (20 of 52)

22/18

GGATGTGGGCGATTTCGACAGCTCTCAGGAACCTACACACTGGTGAG
 GAGGGCCAGGTATGTTCTGACCAGTCACAATCAAAGCAACCTCCCTACTA
 ATCAGGGAGGCTTGGTACCTGGGAATGCTATGTTGAAAGGTTCTTTCT
 GGGTTTAAAATGATGGGCTATTCCTTATTCTTAAGATTGCTTTTTT
 CTGGCTAGAACCTAAAAGAAATTTAGTAAATTCCTCCCTGGCAC
 AAAGTGAGCTGAAATGAATTCCCAGGTGGCCTTGATACTTTAAAATATT
 GCCTCTATAAAATCAACCTTAAAGAAGAAGTCAAAGAACATGCTAG
 ATTTCACAAAGGTTAATTCCTGAAATCCAGTTATCTACAGGACAATGTT
 GTCAAAGAAAAATTATTGGCCAGGCACGGCAGGCTCATGCCTATAATCC
 CAGCACTTGGGAGGCTGAGGCAGGTGATCACCTGAGGTCAAGGAGTTG
 GACCAGCCTGCCAACATGGTGAACACCCATCTACTAAAATACAAAA
 AAAATTAGCCAGGTGTGGTGGGACCTGTAATCCAGTACACGGGA
 GGCTGAGGCAAGGAGAACGCTGAACCCGGGAGGAGGAAGTTGCAAGTGA
 CCAAGTTCAAGCCACTGCACCCCCAGCCTGGCAACAGAGCAAGACTTTGT
 CTCCAAAAAAATTCAATGATATTAAATTCAATGGTAAGGAA
 GATTTCATTAGCAACCAGCACAGAAGATATAGGAAACACTGCAATGGGAC
 TTTGGCGTGGGGAGAGAGATTGAACACAACATACAGCACGGCA
 AGGACATATTCAAGCCAGGAAGCAGAGCAAAGATCAGTGGATGCGAAAT
 TACTAAGAGGAAACATGAAAAATAAGGGAGCTCTGCCTAAACCCACCTA
 ACCGGATCTGCTGAAGACAGGACAGGGTGAATTGGACACCACGGGG
 ATGGTGGAGGATGGGAATCCAGTGAGATTCAAGGGTGAATGGGATATTG
 AACATACAAAGTTCTGCTAAAAAAGGATTACAAGAAAGTGTACAAAT
 GTGCCTGGACAAGGTGCAAGGAGCCGACGGAGATGTGGTCCAGCAGAGA
 ATATGTGCCAGATGATAGGTGAGTTCTGACGAAGGATATATGCTGAT
 CCAGCCAGGGTGAATGCTCAGAGAAAGCACGGAGGGCTATGTCGTTG
 CCCCAGTCTCACCGCGTCAAATCTGATCCCGTTGTGAGTGTGCCGTTT
 GTAGAAAGCAATCAGGGGGGTCCCTCCCC
 >Contig30

AATATATATTTCATANNATNTGAGACAGGTTCTCACTAGGTGCCCAG
 GCTGGTCTTGAATTCTGCCTTCAGTGACTCTCCACCTTAGCCTACTG
 CATAGCTGGGATTACAGGCACAAACCACTGCATGCAGCTAACCTTGCTTC
 TCATTCCAGCACTTTTATTCACTGATTATATGTATATGTATATCTGCA
 TCATCT
 ATGGAAATATCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT
 CAGTCT
 CAACGAGTGTGATGTTGAAATATATATTGTTCTCATCTCTGTTTC
 CTGACATACAGCTTTAAAACCTTGGAAATCTCTGGAAATAAAGAGTG
 TCTTTGCTGCTAATAGATGACTGCTGGCTGGCAGCCCCAATGCAGTAG
 CTTCATGATGGGTTGTCACAGGAAAGACCAAGGCAGGATTGGAGACTT
 GAGACTGTTAGCCCCACTCCCCAACCACTGGAGGGAGTGGAGGGCTGAA
 GGTTGTGTCAGTCACCAATGGCAATGGTTCGGTCAATCATGTTATGTA
 ATAAAGCCACTCTTAAAACCCAAAAGGACAGGGTTGGAGGGCTCCC
 AGATAGCTGGACACATGAAGGTTCTGGAGGGTGGTCCCCAGAGGGCA
 TGGAAGCTCACACCCCCCTCTCACATGCTTGTCTGCGCATCTCTCAT
 CTGGTGTGTCATCTGATCTTTGTAATATCTTTAGAATAACTGGTAAA
 CTTAAGTGTGTTCTGAGTTCTGAGCTGCTCTAGCAAATTCAAGGAAC
 CCGAGGGAAAGCAAACCCAGATTATAGCCATCAGTCAGAACGCTAGGTGA
 CAACCTACCACTGTAACTGGCACCTGAAGTGGAGGCAGTCTGTGAGA
 CTGAGCCCCAACCTGTGGGATCTAACGCTAACCTCAGGTAGATAGTGGT
 GGAGTGAAATTAGGACACCCAACCTGGTGTGGCTGGAGGACTAGTGGT
 GGGAGGAAATCCCCAGCATTCTGGTACTAGAGGTCAAGAGAAACTCAG
 TGTTGAGGTGTTGTGACAGTATGGTAGGGAAACTGCGTCTGGTTTTTC
 CTTTTACAATCAGTTAAATTTAACACAAGTCTACTGTATATTAGTAAA
 AGGGTTACATTTTAATGTCTGACAGTTGCACTTGACAACCTCCATA
 TCAATCACTTTTTCTGTCGTTGGAAACAAAATCACTTGGGATACC
 ATGAACCAAGGCTGAGCGTATTCCCCAGGCCTGAAAGCTTGGAGGCCAT
 TTTGCCAGCCNTAATCCCTGTGAATACCAAGGCTTGTGGATTAAAAAT
 AGACTTGAGGCCAGGCCGGTGGCTCACACCTGTAAGCCCAGCACCTTGG
 GAGGCAGAGGGGGATAGATCACAAAGTTAGGAGTTGAGACCAAGCGTGGC
 CAACATGGTGAACACCCCGTCTACTAAATACAAAAAAATTAGCCG

GGCGTGATTTACACG...AGTAGTGCCAGATACTCAGGAGGCTGAGGLAG
GAGAAATACTTGAACCTGGGAGGCAGAGGTGAAATGAGTCAGAATCGTG
CCACTGCACTCCAGCTGGGCGACAGAGTGAAGACTCAGTTTCAGGGGAG
TTAAAACAATACAAAAAAAGAAAAAGACTTGAACAATGAGGCTCCACTGG
ATGGATTAGGGATTACAGGAAGCAGGACCTGACGGTGCAATGCCACA
CTCCACCTGTCAGAAATTGGACCTCACCAAGGGAGGTCTGTGGGACAGG
GAGAGGCCCTCTGCCTCCACCCCTCCTACTCCCCAACCCCTGAGTCA
GGCTGAATGTAGTAAACCTGGAACAGAAAAGTTCAGTTGGCAATAGGTA
TCTGAAGGACTCCAGGTGCTCTCCCTGATTCAAATTTACTTATAAAA
AAAAATTATAAGAAAATTCTACTAAAAGAAATAATCAGGGAGGTACAAC
AAATTGTACTTTTTTTTTTTTTTTGAAATGGAGTCTCACTG
TTGCCCATGCTGGAGTACAGTAGTGTGATCTGGCTACTGCAACCTCCG
CCTCCTAGGTTCAAGTGAATTCTACTTCAGCCTCCAAGTAGCTGCGA
TTACAGGTGTGACCACACCCGTAATTGGTATTGGTAGAG
ACGGGGTTTCAACATGTTAACCAAGATGGCTCGAACCTCTGACCTCAGG
TGACCCACCTGCCTCAGACTCCAAAGTGTGGGATTACAGGGTGAGCC
ACTAAGCCCAGCATTGTACATATTGTGGGATTACTAAACATTAT
TCAAAATAGTAAAAAAATTGAAATAAACTGGGACTGGTTAATAATT
TTGGGTACAACCACATGATGGAATACTATACAGCCATTAAAATTACATT
GAGGCCAGGTGTGGTGGCTATGCTTGTAACTTAGCAGTTGGGAGGCC
AAAGTGGGAGGATTGCTTGGACCCAGGAGCTAAGACCAGCTGGCAAT
GTGCAAAACCTGTCTAAAAAAAAAAATACAAAAAAATTAAAAAGCT
GGGTGGAGGCACACACCTCTAGTCCCAGCTACTCAAAGGGCTAAGGTG
GGAAGATCACTTGAACCGGGAGGTCAAGGCTGCAGTGACCCAAATCGG
GTCATTGCACTCCAGCCTGGCAACAAAGCAAGACCCGTCTCAAAAAAA
AAAAAAATACATTGAAGAATATCTTACGGTATGGATAAAATATTCAATT
CAGTGATAGATGCAAATAAAAGCAAATTACAAAATATACAGTTAATTCC
AACTTGATACTACATATGTATATATGAATACATGCATATGTTATGTATG
TATATGTAATATAACAATATATGTTCTATATATGGATATTATATTTA
CACATACATACACATATATAATCTTCTCTAGAGAGCAGAAAGAGAG
TAGACAGATAATGAAGAGATAGGATACAACCTCCAGTCCAGCTCAACCTAGGG
GACTTGTAAAGCCTCAGGAGAGAGAAGTGGGACTAGAAAGCAAGGC
AGCTATTGTAAGCATTTGTGTTCTAGCTATTGGGTGGAAACAAAC
AGCACAACTTTGAAAGCCCCCTTCTACTCACCCCAACAAACTGCAGAGCA
GCTTTAGGACCCCTCAGAGTTCAAGAACACATTGCAAGAGTAGAAGAAGT
AAAAACATGTATGAACCTTGACCCCTGAGCTCATGGACTGTGCCATGAGGG
AATTCTAAAACAGCAGGAGAGGCCCTGGAGGAAGGCAGAGGCCCTGCAT
CAGCAAGTCCAGGCAGGCAAAAGCCTGCATTCCATAGATGCTCATCTCTGGC
TGGTGAGGTCTAAAGACGTTGGCTCAATATTAAAGTCTGTGAGAGAGG
TCACAAACCCAGTCCCTGGCCACAAAGGAATAATTCTGGCTTGAGA
CATTAGGGAGGAACAGGGCAAGGGGAGGTCAAGAAAGTTAATGGATG
AGATGATATTAAAGCAAGGCCCTGGAAAATGAGAATTCAACCAATAGCC
ATATGGTAGGTCAGAAAGCAAAAGATAAGGAGGGGCAAGTGCAGGGCA
ACATCAGATATGACCAAGGGTGTGTTGGGATGGCTGATGGAGAAGAAGA
TTAGACTGGAGTTGGGAATGCCACAGTATCGAGGTGGATTAAATCCTA
TGGGTAAATAAGCCAATGTTCAACCCCAACCCACTTGCAATATGGCTC
AAAAATAGCAGGTGTTGATAAAATGACTACTTTACTCTACTATTCCCT
CCCTCTTAAGAAGAAAAGAAAGTGGAGGCTCAGAGAAAGGCAGTGGCTT
GTCCCAATCACACTATGATTGGCCACAAACAAAGAAGCAATGTTACAC
CaaaaaatGCTGCCTCCACCTCCCTCTGCTTCTCCCTGCTGGACT
ACAGACTATCTCAAGAGTGCAGTACACCATCAGGGCTCAGCTTCC
GAAACAATGCCAAAATATTAGCCATACGTCACTGTAGTAAGAGGCCCTGAA
TTGGGAATCCCAGCTTGACGCAGACATGCTGATTGACTCTGTGACCAATT
CTCTTCACTTCTCACTCTATTCTCCCCACCTGTAAGTGAAGGTCTT
CCAGTTATAAAAACAGATGATGCTATTGCTCTGTGTTGTATCTAATCTTG
CTGTGTTATAAAAAGAAGGCTCTGTACATTCTATCTGGCCAATT
CCTCTTATCTCTACTTCCACAGCCCCCTTTCTACAGAAAACCAGCAT
TGTCTTCTGGATCCATCTCTTAAGAAGCGCTTGCCTCCCCGGTTATT
TAGGTGATAAGAAGTGTCTAGATGACAGGCCCTGGAATGGCTGGAGGCC
ACAAAAAAAGCAAGTGAATAGACAGTTACAGCGACGACAATAACAAC

FIG. 3 (22 of 52)

24/118

CAACACCTCTCACTAAAGAGAAAGAAATAAAAAGAAAATTAAAAATCTGC
 CGCAATGCCACACAGTCATTGAATAACTGCATGTACAGCACTGGTT
 ACTTTTACATACTTCATATTTAGCCTCATAGCAGCTCACAGGGGTGGA
 TTTAATTAGTCCAACCTCTGTACGGTGCCTGGCACAAGTATAATAA
 ATGTTCTGTGAATAATGACCCTCTTTAGATGAGGAAATCGAGGCTCA
 AGGAGAACAGCAATGTAATGTCCTCCCTGTACGCCATCTGCCTTC
 ACGCCACTGAATGCAGTAGTCCTCAGTGCCTGAACCTGACCCCTTCTG
 CTTTCGGACTGGCCTCTAATCCCCTGTGACTCACTACACACACCTCT
 CCTGCATATGACATCTACATTAAAACAAACCGTATGGAAATAACACAT
 TAGTCGGCTTGTCCCCACCCCCGCAAAAAAAAGGCTCTTATAACA
 GAAACTCTCAGGCTGGTAGGGAAATTATTCCCCATTATGGTAGAA
 AGGCCCTAACCTTGACCTCACGCCATAGCTATTCACATGGGGAAATGAT
 GAATAACATGGGGAGCAGCATGTAATATCATTGAGCCGTAGTCCAGACC
 TATAACACATC

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GGGGGAGCTGCATGTGCCTGTCGAGATCTGGGGAGGAACAGGAAGATCA
 AGAGTTCTGTAGGACATGTTAAGTGAAGGTGCTTACAGGATAGCCAG
 ATGAAGCATCAGGTGTGCAGTCAAAGATATGAGTCTGGAGCAGCACATCC
 TAAGTCACCTCCTGCACCAACACAGAACATTCCAGGCCACTCACCTGAGCT
 CTCCCAAATAGTTCCAAGTGTCAATTATGTTAATAACCTATGAGCTTGAA
 CACCAAGATTCAAACCCACTGCATGGCTTAAAGACCATCTCAAGGGCT
 TGACACTCCAGGGAGCCAACATAAGATGCCCTGGCTTACCATCAACCTCC
 ACCCCATTTTTATAGAAAATGTTCTACCTGTCTAAGGCAGGGTCTG
 CCCACTCCCAGGGCCCTTAGATCCCCAATATTCTCCCTCCCTGAACCA
 AAACCCATCATCTTCCAGCATGGGTGGGCCTCCATTCTGCTTCTG
 TCCCCTGAGCAGAAGCAAGTTCTCCAACCTGACCTGATTCTCCCTCCTA
 AGTACCAAGTCACTGCTTGTCTGGAAATGAGAGAAAAGACAGAGTGAG
 AGAGACAATCCAGAACCTTGCTCACTCACAGCTAGGCTGGCATCTGGG
 AGGATGGCTGTGCATGGGAACTGGGAAAGCCACACCCCTGGCACCC
 TGGTCACCCACCTGTCTCCCTGGCAGATTCCGCACTGCTCTCTGCACCC
 TCTACCAGGGCTAACCGGCCTGCTCACTCTCCCCAGCATGTCTCCCAG
 CCCACTCTCTAATTATTACATTCCCTCACATAAAACTGCCCTCTCTCCC
 AATCACCAACATGTTCACTTCCCACCCAGCTGTCAAAGTCTGGCTCAACCT
 CATTCTGAAAAGGAAAAAAACAAACAAACAAACAAACAAAGCAAAAA
 ACCTATGATGGATTAAGAACACACTTCATTCCAGGAACATGCTTATCTCC
 TCTAACTCTACAACAACACTACAGCAGGTAGGTGTTATCACACCCATCTCT
 CAGGTGAGAAAACAGGTCAACGAGTGCAGGAGGACACAGCAAGTCAGTG
 ACAAAAGCTTAAATTCAAGCCCAAGCCTGGCAACCAACGTCTGTACCC
 TTGATAGCTACCTCATTACCACCAATCCAGTGGCCTCAGGCTGGCTG
 CACACTGGGATCACCTGGTGCCTCAGGACATCTAGACCAGTCATACAG
 AATCTCTGGGCTGGGATCCTCACGGTACATTAAAGGTCCCCAGGTG
 AGTTCACCATGGACCCAGAATTGAGGACCAATACCGTATACCATCTCC
 TTCTCATCTCTCTAAGGCATCTTACTCGCTGTGCACTCCCATACCA
 CTTGTTCAATCATCCAATCATTCAATTGAGTCAGTTAGTCAGGAGC
 TACTCACTAGTCCCCTGCCAGGTCTAGTCATGACATAGGGCTCTGGGGA
 CCAACAAAGCAGGACCCATGCCCTGCTCATGGAGCTTGCTCTGC
 AGCAGAGGAAGCAGTCAGTGAGATGTGAAATGTGACAGAT
 GGGAAAAGCAAAACTTAAACTTTAGGACAAAATACACAAGAAATCTT
 TGCAACTTGGGACAGGAAGGAACAAACATTCTTACACATGACACCAAAG
 GAATCAACCATAAATAAAAGGTGATCAATTGACCTCATTAAAGTGT
 AGCTTTTTCTTGAGAGACACCATTAAAATTAAAATACATGCCACAA
 ACTGGGATACAATATTACAACACTTATGTCCTCACAAAGGATTAGTTTC
 AGAATATATAAGAAACTCCGGCGGGTATGGCCGCGCACGCTGGAAATCT
 CAGCACTTGGGAGGCCAGCGGATCACATGAGGTCAAGGAGTTCAAGACCA
 GCCTGGCCAACATGGAAAACCTCCGTCTACTAAAAATACAAAAATTAG
 CCAGGCATGGTGGCGGGCGCTGTAATCCCAGCTACTCAGGAAACTGAGG
 CAGGAGAATCACTTGAGGCCAGAAAACAGAAGTTGCAGTGAGCTGAGCTC
 ACATCACTGTAAGCCTCGGTGACAGAGTAAGACTGTCAAAAAACGAAA
 CAAAACAAAACCTCTACAAATAAAATAAGAAAAAAATAGCCCAGCAGGA
 AAAAGTATATACATTCTATAAAAGAATAAAATCATTCTGTCAGTTTCTA

FIG. 3 (23 of 52)

25/18

ACATATATTTTAAGACTAAATAAAATGGTAGGAAACATTTTAAA
ATGCCAACCTCATTAAAAATTATAGAAGTAAAATTAAGCCACAATAAG
ATACGATTTTACCAAATACAGTGTCAACACTTGCAAGTCTGACCTCA
CCAAGTGTACCGACGTGTGCACTGACGTGGCTGCTGAGATACTGATGG
TGGGTCTAAATCTGTACTACAAACATTGCAATAAAATGTAATAATA
TACAATAGGTGGAGCAGGAAGTGACCTGCAACCATAAGCAGATAGGGCA
GGAAAAAGCCTATGAAAGCTGACATCAAAGGGATAAGTCCAGTTACCCA
GCTGAAGGGAAAGGAGGGTGTTCAGATAGAGGAAGGATAAGCATGACCTA
TTCAAGGCCAGTAAAAGAGCTGGATGCAAAGAGCCGTGGGAGACTATTGGGGT
TTAACAGGGATAATAATTATTCATCAAGCATGCACTAAAGGTCACTGG
CACCTGCCATGGGCAGGACTCGGGCTCATGATTGCGTCTGTTGG
AAATATCACCCGGCTGTGAGATGAAAGAACAGGTAGGAGGGTCAAAAAC
TTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTGTGGACTGTG
GCAATCACAGAGGCAGGGATAAAATGCACAGAGACACAAGGCATGTGG
GAGGCAGAAGGAATCAAATACAATGAGTGTAGATGTGGGGTAGAGTG
GTGAGTGTAGAAGACATACTCAAGGTGACACGCCAGGTATCTGGGTGGAT
GGTAAGACATTATGGACTAGGATCGAGGAANGAGGTGGGAATGGGACC
ATACCTGCAGTTATAAGGGTGGACGAGGAAGATTATGCGGGAGACTG
AGAGAGGAATAGACAAAGGAATCCGGTGCAGTATTACAGAAACTGGGT
GGGAGGGGGTTGTANTTCAAAAGAAAAGAAAATTGTCAAATAGTATGAA
ATGCTCAGAGAAACTCACGGATTTTTTAAGCTTAGAATTATTATC
TGACTATGTGAATAAGATAACTTTATGAAAGAAGTTTGCTTAAGTAG
TAGGAAGAAGCAAATTGTTGAGGGCTGATGAGTGGGAGGAGAAGTAATT
GAAGGCACCTTCAAGAGAAACAAGCAGAAGGTGAGGAGAATACTAAT
GAAGGAGTTACGGCCTTCACTATTGTTGCTTAGATAAGCAAGACT
TGAGTGGGTCTGGTGGAGGAGAAACAAGTAGAGTACAAAGTTAAAGGAGAG
ACAGACAGAGATAGAGATAGGGACAGAGAGAGACAGAGACAGAGCACA
AAAGAGCAAGGTCCCTGAGAACACGGGCCTCTGTTAAACCCAGCCAG
ATGTATTGCAATTCAATTCCAGTACTAACCAACCCAGAGTTGTGAGACT
CTACAAGTTAAAGAGCATGGTCCCCAACAAAGACTGCTCTACGTCAAGATG
CCAGGCACACTCAGGGTCCCCAACAGCACTCATGTTTTGAATGACTG
CCATAAGTTCAAAAATTCCCACAATTCTCTCAGATTCAATAACTGGGTAT
AACCACTCATAGAACTCAAGAAAATGCTATCATTATTACAAATT
TATAAAGGATACAAATCAGAAGGACTAGCCAAATGAGGAGACACATAGAG
AGAGGACTAGTAAAAACAGAGCTCTCGCTCACCTCAAGGAATCAG
GATGCACCACTCCCAGCACATCAAGTGTCAACCAGGAAGTTCT
CTGAGCTCAATGTCCAGAGATTAGGGAGGATTCTACATAGGTATC
ATTGATTAAATCATGGCCATGTACTTGAACCTCAATCTCCAGTGTCCCTC
TTCTCCCTAGAGGTCTGAAGGGTGGCTAATATCATGTGGCTCAAAGCC
CAACTCTAATTACCTTTGGCTTTCAAGGACTAGACCCATCTGAA
GCTATCTACAGGCCCTGCCATGAGTTAGCTCTTAAACATAACAAAGACAC
TTATATTACTCAGAAAATTCCAACAGTTAGAAGCTCCATGTCAGGAAC
CTGGGACATAGATCAAATTCTTTTTTTGGAGACAGGGT
CTTGTGTGTGCCAGGCTAGAGTGCACAGACAGATCACAGCTCAATGC
AGCTCAACTTCCCAGGCTTAAGTGCACCTTCCACCTAACCTCCAAGT
ATCTGGGACCACAGAAAATGGCTAATTATCTGGCTGATTTAAACTTT
TTTTTTGTAGGGATGGATGCCCTGTGTTGCCAAGGTTGGCTCAAA
CTCCTGGGTTCAAGCAATCATCTGCCCTGCCCTGTGATGGTTAATAC
TGAGTGTCAACTTGATTGGATTGAAGGATAACAAAGTATTATTTGGGTG
TGTCTGTGAGGGTGTGCCAAGGAGATTACATTGAGTCAGTGGACTGG
GAAAGTCCACCCCTTCCAGTGGACTGGGAGACCCACCTCAATCCAGGT
AAACACAATCTAATCAGCTGCCAGTGTGGTCAGAATAAAAGGAGGCAGAA
GAACAGGGAAACACTAGACTGGCTTAGTCTCCAGCCTACATCTTCTCT
CATGCTGAATGCTTCCATCCCTGAACATCAGCCTCAAGTCTCAGTT
TTTGGACTCTGGACCTCAACCACAGATTGAAGACTGCAGTGTGGCTT
CCCTGTTTGAGGTTGGACTCAGACTGGCTTCCCTGCTCCCTCAGCT
TGCAGATGGCCAATTGTGGGACTTTAACATTGTGATCATGTGAGTCAT
TCCTTAATAAAACTCAGATATATATATGTATCAGACATATATATATC
CTATTGTATATTATACAGATATATAATTACCTATTATACAGATATA

FIG. 3 (24 of 52)

26/118

TAATATCCTATTATATAAGGTATATATATATGTATCATATATA
 TATCCTATTGGTTCTATCCCTTGTGAGAACCTGACTAATACAGCCTCCC
 AAAATGCTGAGATTACAGGGAGCCACAGCCACCATGCCAGCCCCAA
 ATTCTTAATTATACAACAATGGGTCAGAGATCAGGCCTGGTAGGATG
 CAGCAATAAGAAAACAGATGGTGATGGGACACATGTTGAAGTGTGGC
 AGGACATGGCTGAGGGAACTCATAGGATGGTCTATTTCATGGCTGAG
 TGAGGAACAGCATAAGGTCAAATTTCAAGGTCAATGGTAGGTTTA
 AATTGTTGCTGTGAACCCAAAATCTGACCCAGGTCTCAGTTAATTAG
 AAAGTCTATTTCAGGTTGAGAACACCCACCCACTCACGACAAGAGC
 ATCAGGAGGCTGACCACATGTCAGGTAAGGAGCACAGCTTGG
 TTTTATATATTAGGGAGACGTAAGTCATCAATCAATATGTAAGATG
 TACACTGGTCTGCCTAGAAAGGCAGGACAACCTGAAGCAGGGAGGGC
 TTCCATGTCAGGTAAGGTGAGAGACAAACAGTTGCAATTCTTGAGTT
 TGATTATCCTTCCAAGGGCAATCAGATGTCATTATCTCAGTGAG
 CAGAGGGATGACTTGAATAGAAAGACAGGCAGGTTGCCCTAAGAAGTT
 CCCAGCTGACTTTCTTCTAGTTGATTTGGAGGCGCCAAGAGATT
 ATTTCTTACATTCCCCCTTCTTTAAGAATCTTTAAAGAA
 AGCTTTAAAGAAAATGAGTCCTGGTCCAGGTTCATCTGAATTCT
 CGAGGGAGGGATGGTTATCCTAAACGGGTGGTCTGAATTGAGAAAG
 TGCATTGTAC

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AAAAGCCATACGAATGAGGAAGAATTAAGGGCCAGAACAAAAGAAGA
 TGAGGGAAAGTTGAACTTCTTAGAGACTGGCTAAATGGTGTGACCAA
 AATGCTGATAGTGTACGGACAATGAAGTCCAGGTGACAAAGTCTCAGA
 TGGAAATGGGAATTGTTGGGAACTGGGCAAAGGTCCACCCCTGCTATGA
 CTCAGCAAAGAAATTGGGTGCATTGTTCATGTCCTGGGATCTGTGGA
 AGTTGAATGTAAGAGTGATGACTTACGGTAGGGTATCTAGTGGAAAGAAA
 CCTCTAACGCAACAAAGTGTGTTAGAAATTCTTCTTCTTTTT
 TTTTTTTGAGCTGGAGTTGCTGTGTCGCCAGGCTGGAGCGCAGTG
 GCGCAATCTGGCTCACTCAAGCTCTGTCCTGGTCTGCCATTCT
 CCTGCCTCAGCTCCCAAGTAGCTGGACTACAGGCGCTGCCACCATA
 CTGGCTAATTCTTAGTATTCTAGAGACGAGGTTTACCATGTTAGC
 CAAGATGGCTCAATCTGACTCGTGTGACCCGCCCTGGCCTCCC
 AAAATGCTGGGTTACAAGCATGCCACCCGCCCTGGCTTAGAAA
 TTCTAAGCCAGGATATGGCTGCTGCTTCTAACAGCCTGTGCTCAGGG
 GTAAAGAAATGACTTAAAGTGGACCTATGTTAAATGGAAGTAGAGT
 CTAAAAATTGGAAAATTGCAAGCTGGCTTGTGGCAGAGAAAGAATCC
 AAGTAGGCTGCAGAGCAATCATTGCTAGAGAGATTAGCATGACTAAAAGG
 GAGCCAAGTGTAAATTCAAGACAATGTTAAAAGGCCCTGAGGGCATT
 TCAGAGATCTATGAAGCAGGCCCTCCATCACAGGTGCAAGGTTGGT
 CACTAGGCCAGAGGTTTATGGCCANNGCCAGGGCACACTGCTATGC
 ACAGCTTGGACACTGCTGCCGCATCCAGGCCACTCTGCTCTGGCTCC
 ACCCTGGCTCAAACGGCCAAGATAGAGCTTGGACCCTGCTCCGAGG
 GCACAAGCCATAAGCCTGGTGGTCTACAGGTGTTAAGCCTGCAGGT
 GCCAGAATGCAAGATTGAGGGAGCTTGGCACTTCCACCTAAATTCTAG
 AGGATGTGTCAGAAACCTAGGTTCCAGGCAGAACGATGATACAGGGC
 AGAGCCCTTGCAGAGAACCTACTAGGGCAATGCCAAAGGAAAATGTGG
 GGTGGAGTCCTCACACATGGTCCCAGGGCACTACCTGGTGTACT
 GTGGAAATGGGCTGCTGCCCTCAGACCCAGAACGGTAGATGCACTGG
 CAGCTGGCACCTGAGCCTGGAAAAGCTGAGGCAGTCAACTCCACCC
 TGAGATGCCACATGGCTACTCCAGGAAGGCCACAGAGGCAGGGCT
 GTCTAACGGCTTGGAGCCTACCCCTGAAACCAGCTGCAAGGACATGGAA
 TCAAAGATTATGTTGCAAGCTTAAGGCTTAATGTTTCCCTGTCATT
 AGGCTTGTGGACCTGTTGCTTTTTTTTTTTTTGGT
 CACAGGTGTTGAACCAGAACAAATTCCATCTGAATAGGGCTGGTAAA
 ATAAGGCTGAGACCTACTGAGCTGCATTCTAGGAGGTTAGGAATTCTAA
 GTCACAGGAGGAGATAGGAGGTGGCACAAGATAAGGTAGGAAAGACCT
 CGCTGATAAAAATGAGTGCAGTAAAGAACGCCAGCCAAACTCACAAAGCC
 AAAATGGTGTATGGTTGGCTCATGTCCTACCCCAACCTACATCTCAA
 ATTATAATTCCATAATCCCCACATGTTGAGGGAGGACCTGGTGGAGG

FIG. 3 (25 of 52)

27/11/8

TGATTGGATTATGGAGGCATTTCCCCCATGCTGTTCTGGTGTAACTGAG
 TGAGTTCTATAAGATCTAATGGTTTATAAGTGTGGAAGTTCCTCCT
 ACACACATGCTCACACTCTCCTGCAGCTTATGAAGAAGGTACTTGCT
 TTCCCTTCTGCCATGATTGTAAGTTCTGAGGCTTCCAGCTATGCAGA
 ACTGTGAGTCATTAAACCGTTTCTTATACATTACCAAGTCTGGCA
 GTTCTTACAGCAGTGTGAGAACTGCTGGCGATGAGAGTGACCTCTGGTT
 GTGCCACTGCTCATTATATGCTAATTATAATGTATTAGCATGCCAAAAG
 ACACCTCCACCATGACCCCAACAGTCATGCCGTGCCGTCTCAGCACCA
 TGACAGTTACAGATGGCATAGCAACGTCTAAAGGTACCCATATGGAC
 TAACAAGGGGAGGAACCTCAGCTCTGGGAAGTGCCTACCTCGTCCCAG
 AAAGCTGTGAATAATCCACTGCTGTTAACATATAATTAAAGAAATAAC
 TATTAAGCATCCTTAGTCAGCAGCCAAAGCTGCTGTTGCCTATGGAG
 TAGCATTCTTATTCCGTTACTTCTTAATAAAATTGCTTTACTTAC
 TGTATGTAUTCGCCTGGAATTCTTCTGTACGAGGTCAGAGCCCTCTC
 TTGGGTCTGGATCGGACCCCTTCTGGTAACATTTGACCAATTCTCC
 CTTCTGGAATGGGAATGTTACACAATGACTGTATCATTGAATCTTGA
 GAAGTAAATAATTGTTTACTTACAGCCTCATAGGTGGAAGGAAC
 TGACTTGAATTTCAGATGAGACTTTGGACTTTGGACTTTGGGTTGGGG
 CTGGAATGAGTTAAAAGTTGGGGGATTATTGGGAAGGCACGATTTATT
 TTGCAATATGAGAACATGAGATTGGGGACCAAGGGTGGAAATAATA
 TGGTTGGATGTTGCCCTCCAAATCTCACATTGAATGTAATCCCCA
 GTGTTGAAGTGAGGCTGCTGGAAATGTTGGATTACAAGGCTGTCGAG
 CACATTGGATAAGACGTGTAGGNCCC

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CGCAGCTCGCTGGTTAATTCTGGCTCTGTGACCCTATTATAGCACC
 AGGTCTATGACCAGGAGAATTAGACTGGCTTAAATCAGAATAAGAGATT
 TTGCACCTGCAATAGACCTTATGACACCTAACCAACCCATTATTACAA
 TTAAACAGGAACAGAGGGAAACTTTATCCAACCTCACACAAGCTGCTTC
 CTCCAGATCCATGCTTTTGCGTTTATTATTAGAGATGGGGCT
 TCACTATGTTGCCACACTGGACTAAAACCTGGGCTCAAGTGATTGTC
 CTGCCTCAGCCTCTGAATAGCTGGACTACAGGGGATGCCATCACACC
 TAGTTCATTTCTCTATTAAAATATACATGGCTTAAACTCCAACGGGA
 ACCAAAAACATTCAATTGCTAAGAGTCTGGTGTCTACCACCTGAACCTAG
 GCTGGCCACAGGAATTATAAAAGCTGAGAAATTCTTAATAATAGTAACC
 AGGCAACACCATTGAAGGCTCATATGTAAAAATCCATGCCCTCTTCTC
 CCAATCTCATTCCAAACTTAGCCACTGGCTCTGGCTGAGGCTTACG
 CATACTCCCCGGCTTGACACACCTCTCTACAGAAGACACACCTTG
 GGCATATCTACAGAAGACCAGGCTCTCTCTGGCCTTGGTAGAGGGCT
 ACTTTACTGTAACAGGGCCAGGGTGGAGAATTCTCTCTGAAGCTCCATC
 CCCTCTATAGGAAATGTTGACAATTACAGAACAGTAGGAGGATCAAG
 ACTTCTTGCTCAAATACCACTGTTCTCTCTACCCCTGCCCTAAC
 AGGAGCTTGTCACCCCAAACCTCTGAGGTGATTATGCCCTAACAGCAA
 ACTTCCCTCTCAGAAAAGATGGCTATTTCCTCTAACAGTTGGCAGGA
 GCTGCCAAGTATTCTGCAATTCAACCTGGAGCACAATCAACAAATTCA
 CCAGAACACAACACTACAGTACTATTAGAACATTATTATAATAATTCC
 TCTCAAATCTAGCCCCCTGACTTCGGATTTCACGATTCTCCCTCCTC
 CTAGAAACTTGATAAGTTCCCGCGCTCCCTTTCTAAGACTACATGT
 TTGTCATCTATAAGCAAAGGGGTGAATAATGAACCAATCAAAACT
 TCTGGAATATCTGCAAACAAACAATAATATCAGCTATGCCATCTTCACTA
 TTTAGCCAGTATGAGTTGAATGAACATAGAAAAATACAAAACCTGAATT
 CTTCCCTGTAATTCCCCTTGACGACGCACTTGTAGCCACGCTAGCCA
 CGCCTACTTAAGACAATTACAAAAGCGAAGAAGACTGACTCAGGCTTAA
 GCTGCCAGCCAGAGAGGGAGTCATTCACTGGCTTGAGTCAGCAAAGG
 TATTGTCCTCACATCTGGCTATTAAAGTATTCTGTTGTTGTTTTC
 TCTTGCTGTTCTCTCACATTGCCCTCTAAAGCTACAGCCCTCTCC
 TTCTTCTGTCCTCCCTGGTTGGTATGTGACCTAGAACATTACAGTC
 AGATTCAAGAAAATGATTCTCTCATTTGCTGATAAGGACTGATTGTT
 TACTGAGGGACGGCAGAACTAGTTCTATGAGGGCATGGGTGAATACAA
 CTGAGGCTTCTCATGGGAGGGAACTCTACTATCCAAAATTATAGGAGA
 AAATTGAAAATTCCAACCTCTGTCCTCTTACCTCTGTGAAGGCAA

TACCTTATTCTGGTGTTTTGTAACCTCTCAAAACTTCATTGATTG
 AATGCCCTGTTCTGGCAATACATTAGGTTGGGCACATAAGGAATACCAACA
 TAAATAAAACATTCTAAAAGAAGTTACGATCTAATAAAGGAGACAGGTA
 CATAGCAAACTAATTCAAAGGAGCTAGAAGAGATGGAGAAAATGCTGAATGT
 GGACTAAGTCATTCAACAAAGTTTCAGGAAGCACAAGAGGAGGGGCTC
 CCCTCACAGATATCTGGATTAGAGGGCTGGCTGAGCTGATGGTGGCTGGTG
 TTCTCTGTTGCAAAAGTCAGATGGCCAAGGTTCCAGACATGTTGAAGA
 CCTGAAGAACTGTTACAGGTAAGGAATAAGATTATCTTGTGATTTAA
 TGAGGGTTCAAGGCTCACCAAAATCCAGCTAGGCATAACAGTGGCCAGC
 ATGGGGCAGGCCGGCAGAGGTTGTAAGAGATGTGACTAGTCCTGAAGTC
 AGAGCAGGTTAGAGAAGACCCAGAAAAACTAACGATTCAAGCATGTTAAA
 CTGAGATTACATTGGCAGGGAGACGCCATTAGAAAAATTATTTGA
 GGTCTGCTGAGCCCTACATGAATATCAGCATCAACTTAGACACAGCCTCT
 GTTGAGATCACATGCCCTGATATAAGAATGGGTTTACTGGTCCATTCTC
 AGGAAAACCTGATCTCATTCAAGAACAGGAAATGGCTCCACAGCAAGCTG
 GGCATGTGAACTCACATATGCAGGCAAATCTCACTCAGATGTAGAAGAAA
 GGTAAATGAACACAAAGATAAAATTACGGAACATAATTAAACTAACATGAT
 GTTTCATTATCTGTAGTAAATACTAACACAAACTAGGCTGTCAAAATT
 TGCTGGATATTTACTAAGTATAAATTATGAAATCTGTTTAGTGAATA
 CATGAAAGTAATGTGTAACATATAATCTATTGGTTAAAATAAAAGGAA
 GTGCTTCAAAACCTTCTTCTAAAGGAGCTTAACATTCTCCCTGA
 ACTTCAATTAAAGCTCTCAATTGTTAGCCAAGTCAAATTTCAGAT
 AAAGCACAGGTAAGCTAAAGCCGTCTTGATGACTACTAACCTCAGAT
 TAGTAAGATATGAATTACTCTACCTATGTGTATGTGAGAAGTCCTAAA
 TTCAAGAGATGACAGTAATGCCATGTGTATGTGAGAAGCACAACAT
 CATGGTCATTAAAGTACATTGCCAGAGACCACACTGAAATAACAACAAT
 TACATTCTCATCATCTTATTTGACAGTGAAATGAAGAAGACAGTTCCT
 CCATTGATCATCTGTCTGAAATCAGGTAAGCAAATGACTGTAATTCTCA
 TGGGACTGCTATTCTACACAGTGGTTCTCATCCAAAGAGAACAGCAA
 TGACTTGAATCTTAAATACTTTGTTTACCCCTACTAGAGGTCAGAGA
 CCTGCTTTCATTATAAGTGAGACCAGCTGCCCTCTCAAACATAAGTG
 ATGTGCATTGGCTTCTCCCAGAACAGAGCAGAACACTATCCAAATCCCTGA
 GAACCTGGAGCTCCTGGGGCAGGCTTCATCAGGATGTTAGTTATGCCATC
 CTGAGAAAGGCCCGCAGGCCGCTTCACCAGGTGTCGTCTCCTAATGTG
 ATGTGTTGTTGCTCTCTGACACCAGCATCAGAGGTTAGAGAAAGT
 CTCCAAACATGAAGCTGAGAGAGAGGAAGCAAGCCAGTTGAAAGTGGAA
 GTCTACAGCCACTCATCAATCTGTGTTAGTGTGAGGACCAACAAATA
 GACACTATAAGTACTGCCTAGTATGTCTTCAGTACTGGCTTAAAGCTG
 TCCCAAAGGAGTATTTCTAAATTTGAGCATTGTTAAGCAGATT
 TAACCTCTGAGAGGGAACTAATTGAAAGCTACCACTCACTACAATCAT
 TGTTAACCTATTTAGTTACAACATCTCATTGGAGCATGCAAATAATG
 AAAATCTCTAAACATCTTTATCCTGGAAAGGAGGAAG
 GTGAGACAAAGGGAGAGAGGGAGGGAGCCTAATGAAACACCAGTTACC
 TAAGACCAGAACGGAGATCTCCTCACTACCTCTGTTGAATACAGCACCT
 ACTGAAAGAACCTTCATTCCCTGACCATGAAACAGCCTCTCAGCTTCTGTT
 TTCCTTCCCTCACAGAAATCCTCTATCATGTAAGNTATGGCCCACTCCAT
 GAAGGCTGCATGGATCAATCTGTGTCCTGAGTATCTCTGAAACCTCTAA
 AACATCCAAGCTTACCTCAAGGAGAGCATGGTGGTAGTAGCAACCAACG
 GGAAGGTTCTGAAGAAGAGACGGTTGAGTTAAGCCAATCCATCACTGAT
 GATGACCTGGAGGCCATGCCAATGACTCAGAGGAAGGTAAGGGTCAAG
 CACAATAATCTTCTTACAGTTAAGCAAGTAGGGACAGTAGAAT
 TTAGGGAAAATTAAACGTGGAGTCAGAATAACAAGAAGACAACCAAGCA
 TTAGTCTGGTAACTATACAGAGGAAATTAAATTCTCTCCAGGA
 GGGAGAAATGAGCAGTGGCCTGAATCGAGAATACTGCTCACAGCCATTA
 TTCTCTAGCCATATTGTAAGGTCGTGACTTTAGCCTTCAGGAGAA
 AGCAGTAATAAGACCACTTACGAGCTATGTTCTCTCATACTAATGCT
 CTCCTTGGTCATGTTACATAATCTTCTGATTCACTGTTCTACTGTT
 AAAATGGAGATAATCAGAATCCCCACTCATGGATTGTTGAAAGATTA
 AGAGTCTCAGGCTTACAGACTGAGCTAGCTGGCCCTCTGACTGTTAT
 AAAGATTAAATGAGTCACATCCCCACTCTGGACTAGAATAATGCT

FIG. 3 (27 of 52)

29/11/8

GGTACAAAGTAAGCACC AATAAATGTTAGCTATTACTATCATTATTA
 ATTATTTATTTTTTTTGAGATGGAGTCTCACTCTGTTGCCAGGC
 TGGAGTGCAGTGGCGCAATCTTGGCTCACTGCAAGCTCTGCCTCTGGGT
 TCACGCCATTTCTGCCTCAGCCTCCGAGTAGCTGGACAACAGGCAT
 GTGCCACCATGCCAGCTAATTTTGATTTTAGTAGAGATGGGTT
 TCACTGTGAGGCCAGGATGGTCTCTATTCTGATCTCATGATCCGCCT
 GCCTTGGCTCCAAAGTGTGGATTACAGCGTGAGGCCACCGCGCCCG
 GCTATTATTATTACTACTACTACCTATATGAATACTACCA
 GCAACTAATTATTAATGACTGGATTATGTCTAACCTCACAGAACATC
 CTACCTCTCATTTACATAAAAGGAAACTAAGCTCATTGAGATAGGTAA
 ACTGCCAATGGCATACTGTAAAGTGGGAGAGCCTCAAATCTAATTCA
 GTTCTACCTGAGTAAAAAAATCATGGTTCTCCATCCCTTACTGTA
 CAAGCCTCCACATGAACATATAACCAATATTCCTGTTTAAGATAATA
 CCTAAGCAATAACGCATGTTCACCTAGAAGGTTAAAATGTAACACAAT
 ATAAGAAAATAAAATCACTCATATCGTCAGTGAGAGTTACTACTGCCA
 GCACTATGGTATGTTCTTAAATCTTGCTATACACATACATGT
 GAACAAATATGTCTAACATCAAGACCACACTATTTACAACCTTATATCCA
 GCTTTCTGACTTAGCAATGTATTGATGACATTATGCATGCTTAGACCTC
 C

>Contig34

GTATTCTATTCTCGGTTATAACACAAATCACAGTGATTTGTCTATACTTTC
 CAGGATTGTTAATTCACTTCTCAGCTGTTCCCCCTGTTGGCTGGA
 ACTGATTTCTATCTTCTGGAGAATCTCAGCAAGCCAACTCAGGATT
 GTTGGGTGCATTTGTCAAGTCTAGGACCCAGGCTCTGGGTGACTGATT
 CCTCTAATTACCGAGCAATGTAATGAGGAAGTCTGATTGTAAAGGT
 GTTAAACTTTGTGACGGAAAACCTTAATACCATGAATAGAGATTCC
 AGAATTTCACCTCTAACGGGATTCTTCACTCCCTGACATTAGAAT
 GTTAGAAAATCTACCACAAAACATCTGTGAGGCTATCCTACAGGCCGT
 TTTCAAAATAGGTTTACAAGGATTGCTATTGGATGATAGTTCA
 AAAGCGCTATCAAAGTTAATTGATGATGTGCAAGCTGAAAGTTATAT
 GTTAGAACTAGCAGTGATTCAAAAATATCCCTTCTGGCTTTGCTAA
 TATATCTGCTCATTTCAAAGTCCAATATTATAAAACTTTAAAGCA
 GAAAAGAACCTCCATTCTGCTGGCCCCCTCCCTGTTCAACTAAAAA
 GTATTTCAGGCAATGCTATCCAGGACTCACACTCCATCCATCCATC
 ACCTACCATAGTTCTTGAGGGCTCATTCTGAGCGCTTCTGAGTGCC
 TGGGATCTGTTATTCTCCATTCTGCTGCTGCATGGTAGTCAAGTC
 CTCCCTCTTCTCCCTAGGCCATTGAAATCATCTGCTAATTGGTTTCC
 TGATTGCCACGAAACTTCCCTCATCCCTCCTCACATATCAGCCACAGA
 AGTATCTCAAAAGCAAATCTGGTGACATGAAGCCCTGCACAAAACCC
 ATTCAATTACTGGTCCACACCTCCTTGTGGATAAGTCAAGCTCTGAG
 TGTGCAAGCAGGGCCACCTGGAAATCCCCTGCCCTCTCTATCCCA
 CGCATCAATCTCCGTCTATTGCAAGTCTGAAATGTGATATTCTT
 CTAGTCTCTGTGCTTGCATAACCTGTTCTCTGACTGGAAACTCCTT
 CTCCCTCTGTAGTTGGCTAATTCTAGTCTTCAAGACTCAGCTCATG
 CTTCACCCCCCTATAACAAGCTCTTCCCAGCTGGGTGGATGCTC
 CTCTGCTGTGAGTCTGAAACATCCTCAGCAAACCTCAGCTTGTCTT
 GCTTGTCTCCCTGCTGTCATGCACCTGATTAGGGCTGGCATATACTG
 TTCACTCCATGACTGGCTCATGGTGGCTCCGTGAATATCATCCACCC
 AAACGGATGAGAGCTACCATGCCATCACTGTGACTTCCATCTGGAGCTA
 ACCTCCCCCGACAGGAAAGCGTTCTTAGGAAAGAATATCTTGGGTTA
 AATAGAAGTAGAGACTCACCAGAACACTATGTCCAGCTCAGAAATGAAC
 GCTCAGTAAGCAGCCTGTCAATGAGGAGGAGCAGCAGGCCAGCCCCAGAGG
 CCTCAAAGTGGAGAGTAGAGAGAACCGCAGTCTCTGCCACAAAGGCACAGT
 GGACACCTGCTCCCTGGCTGGCTGGAAGCAGATGGTGTCCACCTGCTT
 CCATGGGAATTCTGCACCTTAATAAAGTTTATGGGACAGGAAGGTGAC
 TGGCATTGACATTGTAACGAGGAATGGGTGGTGCACCTTGTGTCT
 TACCAAGAAATACCTGTGGCAGGTAAATTCTAGAGAGACCCCTCCATTTC
 TCCCATATAGCAATTGAAATGTTCTGAGGGCTTCCAAATTCTAC
 GGGAACATAGGAGTCCAGAAAGATGAAATCAAAGGTGATGGTATGCCAA
 AGAAAGTAGCTTTAGAATGACTTACATTAGCCATTCCATTAGCAC

FIG. 3 (28 of 52)

30/118

ACCAGGCATTCA G T T G A G G G G T G T G T G T G C G C G C G C G C G A G
 CGTGCATGAGTCATGCGCGCGTGTACATAGGGAAAGGGAAACAAAAC
 AAAAGTACACAAGACATGATAGTTGTCCTCAAGGAGTTTTGCAAATGTT
 CACAATTAAAGAGAATATGCTGTGCTGGCTGGTGTATAAACCAACTGC
 TAGGGAGAGGCCCTCCACACACACTTGGGCAAATGCGACCTCTAGGACT
 GCCAGTGGAACTCTGGGATGCTGTTGTGGCGATAAACCCCTGGTCCCTT
 GATCAGGGACCTATGTTACTTTCTCTCCCTGGAAGTCTTCATTAGTG
 GGCATCCAGAAGGTCTTGACAGGGCAGAGGGAGGCACAAAGACAAGAGT
 TTGAAACCAGCCCTGGACAACAAAATGAGTTCTATCTTACAAAAAAAT
 TTTAAAAAAATTAGCCAGGTAGGATTGCATGTGCCTGTAGTCCCAGCTAT
 TCAGGAAGCTGAGGCAGGAGGATCCCTGAGACCAGGAATTGAGGCTG
 CAGTGAGCTATTAAGTTGGCGAAAAGTAATCGTGGTTTATCATTAAA
 AGTAATGGCAAAACTTTAATGACAAAACCGTGAATTACTTTGCACCAA
 TTTAATATGATTGCACGACTGCACGTGCTCCAGCCTGGCAACAGAGTG
 GGACCCCTGTCAACAAAATAATAAAATAAAATGTAACATGTAAAAAA
 ACCCCAAAAACAAAAAAATGGGTGTTGAGACCCCTGAATTGAGGAATAA
 TAGGAAGGGAGTGTGATTCTGTGTCATGCATGGGTGTCACCCCTCAGT
 GCCTGGGTGGCTTACCCCTGGCTAGTTCAAGGTGGCAAATGGTTTCTCC
 AGCTGGGCTACCAACATCTTCCCCCAGGGCCTGTCCATGTATTGGTGGC
 AAGATAACCTATGGACTAGAGTCCCTCTCAGAGGAAGGCTCCCTCATT
 TCTCTGGCTTCAAGGTAGTAGTCATGACTCAACAGGTCCCCACTGCAA
 TGTATGGGTAGTTAGGTGGGGTCTCCTCTGAGAGGCCTCCCATAGCCC
 AAAAGGCCCTGTCTAGCTGGCACTGCATCTCCCTCTCCAGCTCTCAG
 CCTTCTCTTGTCTCATCCCACTCCGACAGGCTTCTGCCTGATCCTTG
 GATGTGTCAATCCTGCCCTAAGGGATGCAAGGCAATTGTCTTTTATT
 ATTAAGATCTCTCCTGAGGCCACGTGTGGCTCACACCTGTAGTCCTA
 GAACCTTGGTAGGCAAGGTAGGAGAATTGCTTGAGCTCAGGAGTTCCAG
 GCTGTAGTGAACCATGATTGCAACCATTGCAATTCCAGCCTGTGACACAG
 CGAGACCCCTGTCTTTCTTTCTTTGAGACAGGGTCTCGCTCTGT
 CATCCAGGCTAGAGTGCAGCGGTGTTCTGCTCACTGCAGCCTCAACC
 TGCAACATTGTTGTAGAGACGGTGTCTTGTATGTTGCCAGAGTGGCCT
 CAAACTCCTGGGCTCAAGAGATCTTCCACCTCAGCCTCCAAAGTGTGCTG
 GGACTACAGGCCTGAGCTACCGCGCCCAACAAAGACCCCTGTCTAAAAAG
 AAAACAAAAATAAAACAACCTCCCTCAAGTCTTTTTTTTGAGACGG
 AGTCTCGCTCTGTCGCCAGGCTGGAGGGCAGTGGCGCAATCTGGCTCA
 CTGCAAGCTCTGCTCCGGTTCACGCCATTCTGCCTCAGCCTCCC
 GAGTAGCTGGACTACAGGTGCCGCCACACGCCTGGCTAATATTGT
 ATTGTTAGTAGAGATGGGTTCACTGCCTTAGCCAGGATGGTCTTGATC
 TCCTCACCTTGTGATCCGCCGCCCTCGGCCTCCAAAGTGTGGGATTAC
 AGGCATGAGCCACCGCGCCAGCCAGACCTCTTGAGTCTAAACTCCTCT
 GTAGTCCAGCCACCCCTTAGCACATGACTCTGTTAATTGTTCTCACT
 GTCTGAAATCATCTCCTGTCACTTGTACTGACAGGTCTCTGCACTAGC
 CCACGTCTTAATCAGAGTAGGTCCCTGTCAACTTATTGATATTGTGCTCC
 CATGCCAGTGTGGATGATTAAATTGTTGAGTGGAGGCTGATCAGATGAG
 CCATCTCTCCAAGTCTCACTTGTGGCTCCGTCTTAGTTAGTCC
 CCATTCTCAAAGAACGTGAGCCCTGGAAAGTATTAGTCATTTAGTTC
 AGTGCCTTGGATGGGAGGATCACATCCCTGGTCCCGTCTGCAGACTG
 TTTGCTCTAGCTGACTAGGCAGGATTCCCTGCCTCTCACTCGGCA
 TGGGACTTCTCTGAAATTGCTGCTCAGTCAGCAAGAGAATGACCTCCCCA
 ACATAATCCTACTCCACAGGGACTTAAAGGTGTGTCAGAGATCTCTGCT
 CATCTTCTGGCCAGGTGCCACGTCAGTTATAGCCAAGGGACAAGACT
 AGTTAGCAGATCAGGCAGGTCTTAGACCCAGCGTAAGTGCCAGACTTCT
 AGCTGCAGTTGTTCTGCCACACTGGCGTTCAGGTGGAGAGAGGGCAT
 GGCACACTGAGCTCTGGCAGGACTCTGAAATCTCGGTGT
 CAGCCACAGGCCACTCTTCAAGCAGGACTTCAGTCAGTCAGTCTGTCACTAG
 GCTGTGAGCACATGGTAGGCTTACCCC
 >Contig35
 AAGGAGTGTGCTGATAGCATGTGTGANGGGACGAGGAGTAAATAAT
 TTCTGCCTTCAAGAAATTGCAAACACTAGTAATGGAGATAAAATCAACAGAG
 GAACAATTAGAGTATAAGGTAAAATCTAAGGGCATAAGAGAGGGAGAAGA

FIG. 3 (29 of 52)

31/11/8

AGTATGGGAGTTAGAGGTAAGGGGTAAATGAGGGGAGTAGGTGGGTAGA
 AAAGGTTAAAAGTAAATAATGATGGAAGGAAGACAAAAAGACGACAGGG
 GTGCCAAAGGACTCTAACCTCATCTGAACGGAGTTGCCCTGTTTGCTC
 TCTGATGCTCATGTATCTATCCTAGAGACAGCTTGGCGGGCAATGTAGA
 GCGTAGGGGCTGACATAGGGGTTGGAGTCCACCTCCGTGACTCTAGC
 AAATTAGCAAACCTTGCTGCTAAGCCTATAAGGCCGACAGAAATGCC
 ATCTTAAAGCTTGTATGTAAAGTGCCTAGGACCTCGTAGGCATCAACA
 GGAATAATGGATGAAACAAAACAACGGTGCATCTGGAGAAAGTGGCA
 TCTGAGCAGGAGTATTTGAAAGGTAGGAAAGGGCTCCAAGCACATCTAA
 GAGATTAGGGAACGCAGAAGCCTAGCCCTGGGTGCAGATTAAACCAATC
 AACTCTAACCAACCGCAGGCTGAGAGGTGTGGAGTGAGAGGCCGCCAGA
 GGCAGGGAGACCCGGGCTTCGGCCAGACCCGCCCTGGTACAGAGGACC
 ACGCCCGGCTCTGCCCTGGAGCCAAATGTGGATCAAACAGCGCAGCTT
 CCCACTGCTGGTGAACCCGAGCAAGGGCCTCAGTTCTTATCCGA
 ACGTGGTGACAATGACATCTTGCAGGCTGCTGCAGGGCTTCTGGA
 AATAACGCCGTGAGGTATCTGGGCTGCGCACAGCCTCCCCGCCAGGA
 CCCAGACGTCTACCTGGGGTCTCGCCTCCCAGGATGGAAAACGC
 CCAGGGAAACTTAGGCAGCGAGCGGACGGCACCTCCCGGGACGAA
 CTCACTCGGTGGCCTCCTACTTCCCCGGCGTGTCCAACGCCCTGAGAAT
 AACGGGACAGCGGTGCTACTCACCGACAGCGGAGCAGCGGTAGGCCG
 GGCCCCACCATGACTCTCAGTGCAGCTTTCTCAAACGCCSCTG
 TAGCCAGGACCGGCGTGGCGCGTCCACGCGCTCTCATTGGCTCTGCG
 GGTTGAAACTCGCTAGTCAGCACGGAGGGCGGGACAACAGGCAAT
 AGGCTTTGCGGTTGGCTCTGGCCTTGAGAACCCGACCTTGGGCCCTT
 TGATTGGAAGAACGTGCAGCGCACCTCGGCATTGAGGGCGCTTCTCGG
 GGC CGGGCGCCGCCCTCTGAGTGCCTGTGAGTGCCTCCGAGTG
 GGC GTGGGACCCCTCCGTGGGGCGCTCAGCCGGCTGGGGTTGGGGCG
 GTTACGCTGAATCCAGCTGGGTTGGCGCGCCGGAGTCCCTGGCGGAG
 AGACAGGGCGGTCTCCAGGATGCTGGGGCGCTACCTGATTCTGCTCT
 TTCAAAGTCTCAGACTCACAGGAGCTGTGAAAAAATAATTAAAGAG
 GACATATGGGCTTATGCATCTAAAGGCTCTAGTTCTAGTACTGCAGG
 GTGGCTGTTAATGTGGTAAATATGCATAACATCACATACATACATT
 TAACCATTAAAGTGTAAAATTTCAAAATGTGCAGTTAGTGGTAT
 TAAGTACCCCTCACATTGTTGGCACAGCCACCAACTGTCTTTCCAGAAC
 TTTTCATCTTCCCAAATGAAACCCCTGTACCCGTCACTAACTCCGCACTC
 CTCCCTCCCCCAGCCCCAGGCAATCACCATTCTAGTTCTGTCTATGG
 ATTTGACAACCTGTAGGTGCCATATAAGTAGAATCATGCAGTATTGTTCT
 GTGACTGGCTTGTTCACCTAGCATAAAGTATTCAAGGTTCATCCATGTG
 TAGCATGTGTAGAATTCTTCTTTAAGGGGAATAGCATTTCGTT
 GTGTGGAGATGGCACATTGCTTGTCCATCCCTCCGGACACTT
 GAGTTGCTCCACTTTGGCTATTGTGAATAATAATGAACATGAATG
 CACAAATAACTTTGAGACTCTCTTTCAATTCTTTGGGTATATACCA
 CGAAGTGGTATTGGATCAAACGGCAATTCTATTAAATTGGAG
 AAACGTGCTTACTCCTCTCACGGTATCTCTGTCAAGGTATAATTTCG
 ATTTCACCTGATCAGCTGACTATAAGGCCATAAGGCTAACGGAGAACGC
 AGGCTAGTTCTCTAGTTACTAGGAGATCGCAGGCCCTGTTGCTCTGA
 ATCCCTAGACACACTTCATTCCCTTGTTAATCTAAATTCTTCT
 TTTGAAGTTGTCCTGTTCATCTATTCTCCAGTTCTTAAAGAGGTCTG
 GAAAATGCTTTGGCTCTGTATGAAGGTTCTCTTCCATGGATGCT
 GGAGAAGTCGTGTGGAGGGCAGTCATATCTGGCACCTGTTGGCCAG
 GTTCAGCTTACAGTTGGGTACTCAGCAGGGCATGAAGCCACTGCAGCAG
 CCCTCTCTTGTGGTAAATAGGGAGTTGGAGAGAGGCCAGGGTTCT
 GGATTATGCTATTGATATTTCATAGTGTATTAATGTTAAATAG
 GAAAATGATCATTATTGTTAATGACTGAGAAAGGGACTCCTTCACC
 AACAGTTCAAGAAAAGTGAAGGCGGTTTGTGTTGGTCTTGTAGAATCT
 AGGTGGGTTGAATGCATGTCAGTTGAGAAGTCACCTGGCTGATATCCCA
 CGCAGTGCCTGGAGTATTCCACAGACCCCATGTTAGGACTGCACCTTGCA
 GGTATACTGCTGGTGTGGTGGAGCTGCCTTACCTGTCTGTTATTGGAGA
 CCCCTGCTTATTAGGAAACTTAAATGAACTCAAATGAGCTCCTTGCTT
 ACTGGTCTTAGTCCTTGGAGCAACATAGGCCAGTTCTGCCTCGTTTTT

FIG. 3 (30 of 52)

32/118

TCCATCCTTGGGTATTCACGGTCTATTTGAGGACACAAAATGTGGG
 AAAATAGCTAGGCAGGTTAAAAATTCTCAACTCTACCAAGCATGGTGGC
 TTATGTCGTAACTCAATCCCAGCACTTGTGAAGCTGAGGCAAGAGGATT
 GCTTGAGCCTAGGAGTTGAGACCAGACTGGCAACATAGCAAGACCTCG
 TTTCTTAAAAAAATTACAAAATTAAACCAAGGCATGGTGGCA
 CACACCTGTAGTCCCTACTCAGGAGGCTGAGGTGGGAGGATCACTTG
 AGCCCCAAAGTGAAGGATGCAGTCAGTGCAGTGTGGCATGCCACCGCACTCC
 AGCATGGGAGGCAGAGCAAGACCCGTCTCCAATAAATACATAAATTAA
 ATTCTTAACCTCATCATAAGTATCCACTGTAGCTTCCATCATCCTGG
 TGTTGTTTTTTAGAAGGATCTGGCTCATTGCCCGCTAGAGTGCAGT
 GGCATGATCTCAGCTCACTGCAGCCCCACCTCTGGCTTAAGCGATCA
 CCCACTTCAGTCACCCATCTGGTAATTTGTATTTTAGAGATGG
 GGTTTGCATGTTGCCAGGTTGGCTTGAACCTGGCTCAAGCGAT
 CCATCTGCCCTCATCTCAAAGTGTGGGATTACAGGTGTGAGCCACCA
 CACCAGGACAATCCTGGGCTTTAACGGTTTACTCCCTCAGGCT
 AATGACCTATAAGCCCCTGCGGGCTTGGCCTTTACTCCCTCAGGCT
 CCACCTCCCTAGCCTAGCCCACACTACTCTCCCTGCTCAGTGTAT
 CCAGACACTTGTCTTCCATCTCTGTGGGAAATCCA
 ACCTTTCTTCATTTCTAGTGTGATTATTATTATTTACTCTAGCA
 GCCTTATTGAGATTTACATACCGTACGATTCTCCACTTACAGTGTAC
 AATTCAATTCTAACATTTCATCACCCCCCTAAAGAAACCCCTATACTCA
 TTAGCAGTCACCCCCATTCTCCCTCTCAGCCCCCTAGAAACCATGA
 ATCTACTATCCATCTCTATAGATTGCCTCTGGACATTCTATGTATG
 AAATTATGCAATTGTGGCTCTGTGATGGGCTCTTTGTTACCAAAATAT
 CATGGGTTGATCTAGGCTCTGCTGCTGACAGAAAAGCCAGCCACT
 GAGATGACAAGTATTGCAAGGAAGAAGGCTTAGTCAGGTGCTGCAGCT
 GAGGAGATGGGGCTCAATCTCAAATCCATCTCGTGAACCTAAAACCAGG
 GGTTGGATAGCAGGGAGAATGTAACAATGCGTAAGAAAACAGGAACC
 AGGGAGGGCAAGGAAGCAATCTGATGAATGAGTGGTCAAAGTCTCAT
 TGCCCTGGATGTGGTATCTGGGAGTTCACTTCTGTTGATACTTTTG
 AGAGGGCTGAAGTCTTCCCCAGGAAGGAACTCAAACAAAACAAATACA
 AGCTTCCAGCTTAAGACCAGAAGCGTCAATTCTATGTTATCCGAAAG
 AACAGTCTATGGGACTATTGGTAAGTTCACTTCACTTAGTATGCTGT
 TTCAAGGTTATCCACATAGCATGTGTCAGTACTTCATTCTTATGAC
 TGGGTATTCTATTGTGCCGATATAACATATTATTGCCATTCTCATCAGT
 TGATGGACATCTAGGTTCTTCACTTTGGCTATTATGAATAATGCTG
 TTATGAACTTCATGTATAAGTTGTGAGACATATGTTTCAACACT
 CATGGGTATATACTTAATGAGAGGAATTACTGTGTCAGATAATTCTA
 TCTTAAACCATTTGAGGAACTGCCAGACTGTCTTCAAAGCAGCTGCAGC
 ATTTACATCTACCAGCAGTGTATGAAAGTCCAGTTCTTACATCC
 TCAACAAACACTGTATTGTCATCTTAAATTACAACCATCCTAGTGG
 TTGTGAAATGGTATCACATTGTGGTTTATTGTATTCTTGTGACT
 AATGATGTTAACGATCTTTATGTGTTACTGCCATTGTATATCTCT
 ATTCAAGAGTCTTGCAATTAAATTGGGTAGTTGCTTCTTCTTCTT
 TTTTTGAGATGGAGCCTCACTCTGTTCCAGCTGGAATAACAGTGGTGT
 GATCTCAGCTACTGCAACTTCCACCTCTGTGTTCAAGTGTGATTCTGGTGT
 CCTCAGCCTCCAAAGTAGCTGGGATTACAGGCACCTGCCACCATTCCAG
 CTAATTCTTCTTGTATTGAGTAGAGACGGGTTTACCATGTTGG
 CCAGGCTAGTCTCTTGTGACTCTAACCATCCTCAGTCTCAGACAAA
 ACATCCCTTCTCAAGGATTGTGATTAGCTTGTATTGCTTATCTTC
 TCCCTGCTAGTCTGAAACTGAGGGTAGGCCACTATATTCAATTGTTCTG
 GCACCAAATAGAAACTAAATTATGCTTTGAATGAATAGGGCTTCTC
 CTTTAAAGATCCCTCAATACAGTAACCACACTATATATAAGTAGGCCAC
 AAGCCCATTCAATAACTACTAGTNCTTGCGCCAAACC
 >Contig36
 GGCTCAGCGTTACTATACTGGTCTCAAACCTCTGGCTCAAGCGATCTGC
 CCCCCCTGGCTCCAAAGTGTGGGATTATAGGCGTGGCCACGGTGCC
 TGGCCTCAAATAACTATTAAAGTGAACAAAACAGTGTGACTAATGA
 AAAATGTTAAAGTCAAACAGACAAAAGACAATGACAAAACCTTAATGCAATG
 TTATGTTAAAGTCAAACAGACAAAAGACAATGACAAAACCTTAATGCAATG

FIG. 3 (31 of 52)

33/18

AACACTTTGATTAATGAACATAATTGGATATGTACCAAGAATTAGA
 GAATACATACTAGTTTGAGTTATGCAGAACATTACAAAAATTAGTG
 GAAGCCTAAATTATAAAAAGTGTGTCACGTAGAATAACACACAAACCC
 CTGAGTCGGAATTCAAAGCCCTCACACTCTCCTCTACCTTGATCTT
 TATCCTCCACCACTGCAGTGCATACTCTGGCTACTACTCACTGTTCT
 TGATTCAAATTCCATGTTCTGTCAAGCTCAAATCATTCTCTGCCTGGAA
 TAATCTACTTCATACATATTCTGTATTGAATTCTGTCTTAGCACCCCCAT
 CTACTCCAAGACGATGTCCAGTGGGGTACTCCCTGTCCTATTCTTCTT
 GATTACACTTTTTCTACTTCATTATATTGATCACATCTGTGC
 CACAGTTTGACTTTGTGCTGCTTTACTCTTCTAGACCCGTAG
 CTCCTGAAGGGTGGGTATTCTTTTATTGCTCATCCTCATGGCA
 CAGTGAAGTGTAAATAAATGGCTATTGACTGAAATTAAACTGTATCTAA
 TGGACATATTCCACTTCTGGGCCATTCAATTCTTCTTCTATTGGAACCA
 GGAGATGGGAACCATAACAAAGGTAAAGGTTGCCATGTGAAAGAACAT
 GGAACCTTCCCCTGAGGCCAAAAAAGAGCAGGGAAAGGTGCAAAGACAA
 AATCTCCATTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGG
 TGGGACTTTATCATGACGTTATTGGGGACTTATAGCTGCATCATTA
 CCCCATAACATTACCTTACCTTACGTTAGGAACTGAGGACAGGAATTGTTG
 TGATGCAGACTCTGCTAATGAGGCTAACACTGGAGAATTATCATG
 CATTCAAGAAGCTGTTTACATTCTCATTAAACTTTAGTTGGTGGT
 TTAGCTTAGTTGAGGCTTATCAGATATTGGAGATATCTCATTAACG
 ATGGCTTGGTTTAAAGAGTTATTCTGAAGCTACTATTCTGGCAATA
 ATCAAACAGCATGGCATTGTTGTAAGGCCCTCTAGAATATGACG
 GTAAAATCTACGTGTGGAAAATGCTTATTCTCTGTCCTCTATAATGT
 GAATCTAGTTGTCTTCAAAATGAAATCAAGTGAATTAAATGTAGTTTC
 TAAGAAGATAAAATGGGAGCAAGCAGCTGTGTTCACAGTGTGAAATC
 ACTCATCCCTATAAAACTGTCCCAACTGATCCTGACTCACATGAATGAA
 TTAAAATAAGAGTTAAATAACATCAATTACATTAAAGACACTTCCC
 ATGTTTAAAGACTATTGGTTGGAAAAGCTGGTAGGTGACAATTGGAG
 AGTTGGCTGTTTGTCTGCTGTTGACGTATTCAAGCCATATCT
 AATTGTTGTCAGAATGGCTGAATTCTACAAAAATGTTGAGTTGTGAG
 TGTGGAGAAGTACGGAGCCATTACTGAAAGGCTGGGGGAAATGACGAG
 ACCCTGAGATAAGGAGTAGTGGTGCAGACAGAGTGGAGGGAGGTAGTT
 GAGATATGTTAGAGTAGAATCAGAATGGACATAGTGAACAACTGGATGC
 AGGTGGGGCTGAGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGT
 TGATCCACTGAAGTTACATTATTCAACACCAAGGAAACTAGGGAAATG
 AGAAGGCATACTGGTTGCTTGGAGTGGAGGGCAGTGAATGTAAGAGGA
 GTTAATGAGTTAAAGTTGGATATGCCACTTCAATTGATATGTGCA
 TCTGATAACCCCTGGGGTGAACCTCCAGGCAATGGTTGAACATGTGTAT
 TTCTTAGTAACGTAGGCATCACAGACTCACATCAGTAAGGAAGCAACA
 GCAAACCTGATTGGACGATACCTGAACTCAGTACCCCTATGACTGGAG
 CAAGTCTCTGTCAGTGAATGAGGATAAGAAGAATCTTGACCTTGTGGAA
 TATGTTGTTAGGAATATATGTGATGAACAAACATAGGAACTTCCCTACAGG
 GCTCCACATGTAGTAAGGGCTTATAAAATGCTGATAAAATATTGTTG
 TAATTAAATTCCAAAGTAAGATGCCACTGGAGGAATTGGAAACCCAAA
 TTAATAACAAATAGGACTGGATGCAATGGCTCACACCTGAACTCCAGCA
 CTTTGGAAAGGCCAAGGAGGAGGATCTTGTATCTGAGGCCAGAAATTCAAGACC
 AGCCTGGGTGACACAGGGAGACCTGTATCTGAGAAGAATTAAAAAAAT
 TAACCAAGATGGGGTGGTGCACGCCATTAGTCCCTGCTGCTTGAGAGGCTG
 AGGTGGGAGGATTGCTTGAGGCCATGAGGTTGAGGCTGCAGTGAGGCCATA
 ATTGTGCCACACACTCCAGACTGGGTGACAGAGTGAAGACCCCTATCTCAA
 ATAATAAAATAATAATAAAATAAGTACAAACAGCAAACACTAAT
 CCTTCTAGAGATTATTGAACTCTGGAGGGCAGATCTGAAATGGAGGCCAGC
 AGAGGGACCTATGGAGATCAGCCTGGCCCTGGACAGCACCGAGCAATGGG
 GTTGCTAGAGAGGTAATGGGTTGAACAGGGTTAAGGCATGAGGCTCA
 AGAATCCGTGAAGACTCAGACTAATTCTTGTATCTGAGGATTAG
 GTGTTCTAGGAATTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGT
 AGGAGAGCTGAGGGAAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGC
 GTCAAGTATGGCTCACCTGCTTTCTTGTATCTACTTAGCAGATGATCCCA
 CCCAGGCCTCAGGGCAAGGTCAATTCCACATAGTCATGGGCCCTTGA

FIG. 3 (32 of 52)

34/118

GGGCTGGAGCAGTGTAA...GAAGACAGAGTCTTAAGAAATTGCAATTAAAC.
 GTCATGGTCTGGCAAGTGTGTCATCCTATGCCAACGCTGATCTGAAG
 GGGTGCATGCTCATAGGTAGCTGCTGCCAAGATTACAGCAGCTCTTCA
 ATCCCAGATCCATGCTCTCCTATATTCACTTTCCAGGGGTTCTGTCT
 TCGACAGTGTAGAGATGAGAATGACTTATTGAGTTATTCTCTGATAGT
 TGCCAACCTTTCCAATGACAATGGGATGGAGCTTGGAGAGTGAAATG
 AGGCCTAGGGATAGCGTCTTAGGAAAACACTCCCAGCCTGATGTAATT
 CTGGGGTACAATGGCATTTCATCAAGACTGATGTAAGGGTGA
 AGCAGTGTAGTTGGGGTACTCGCATGGGCTAGGTTCTGATCTGCC
 TAATCCAGACAGAGCAGAACACTAGTGGCTGGTAGAGGGCCTCAGGG
 CCTCACTTAATGCTCTGGAAAAACAGCTCCAGATTGTTGGTCACGTTCT
 GAGGACAAGCTGGGTACTACAGGATAGAGAGAGTGGGGAGATGCCGT
 GGCCTGCCCTGCTGATGCCCTGCCATTCTCGTGTGATGTCCTG
 GGGCATCTGGCTTCCCTGCCAGACCTGTAGTTCTGAGGGCATGTG
 GAGGCAAATGGCTCTTAGAGTGTACTTCTGAAACAGCTGCTGG
 GAGAACTGGAGGAGCTAGCTAGTCACGGTAACGAGCAGTCAGGATC
 GTCCCGGTGGAGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTT
 TTCCCTGGAGATGTGTGGCATGTCTAGAGGAATAACCAATTCTGAG
 CCTTGAGCCCTCCAGGAAACCTTGGAAATTAGGTTAGTCATCCCCAAGG
 AAGTCTAAGAAATTCTGGTCTCACCCATCTCTTAAATTCCCACAATGATC
 CTACATGATATTAAAGGAACACGGGCCAGTAACCGTCCAAGCAATGGATGT
 GGTGGTGAAGTTGACCTCATGATGGAGCGAGGTGTTGAAACCTAA
 GAATTAAATTATTGTTCAAACCTGTTCTCACTCAGCGTTATTAAAGCA
 TACATAATTGACACATAAAATTGTATATGTCACGGTGTACAATGTGAT
 GTTTCGATCTATGTATACATTGTGAAATGATTACAACAAGCTAAATAACA
 TACCACATTCACTGTGTTCAAAGGAATTAAACTCAAGCACAAAAGAGAGG
 TGCTGTTGAAGAGTAGGGCTGCTCTAAGTAGTAGTATGTCAGGGTTGT
 CCTGGATCAGGGCTTTGTGCTAGTAATAAACAGGCCCTCTGGGGCT
 GCTCCACTTCCCCACATTCTCTGGAGCCTCCCTAAGAATTAGGACA
 TGGCCACTTCTGCATAGGCTCTACTCAACAAAGGACAGGGCTTGT
 GCTGCCCATGCCACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACAC
 TGGCTGAGTGGAAATCCCCCAGATTACCTGGTTCTAAGCATCATGG
 CTGTATTCACACGTATATGAAATTACAATTACAGCATAGTCGAATAAGG
 ATTGTTGTGCTACAACCTGGAATCCAGATTATGCAAATTGGATAGTATAA
 TATTGAAATTCTCTAGGACTTTTATTAGTTAAAAAATTATACAAGCTT
 AGAGTAAGAAATTAAACAGTCAAAAGAATTCACTGTGAAAGTAAATG
 CTCTGTCCTGCTGAGAGACAGATATTGAGCAGCCAGATACTACTGGGTG
 AATAGTTCTTTAAGCATGCCATTGATGGTTATGGACTTACAGCT
 CAAGAAGCTGACACTAGGGTTGATCTCAGAAAATCATTGTTGAGGTAT
 TAGATACTACCGTCTCATAAAGATACACACACAGACACAGCGATTGGAGA
 TATTCACTGGGCTTATGGCTGCTGCTCTGCTGTGCTTAAGT
 TGGGCTCAGAGTAGCCTGGCATCGGCTGTGGGAGAATGCTGGCATGGGG
 TTAGCAGGAGCCCACTTAACATGCTCTAAGCCACCTGGAAGAGTCCTTCA
 AGGAGACAGACTCCAGAGGCCCTAAGGAAGGAAGGACTTTGCCGTTT
 TTAGGTATTCTAGTCCCAGAGTTAGGGAGGAATGGTTGGCTTGGTC
 GTGTGCCCTTACCGAGTGGATGGGATGGATGTGCCATGAGCTGTTGAGCT
 GGCTCTGGAGAAGACAGCAAAAGCGGAAATAAGAGGTCAGGAAGGCTGTG
 TGGTTGAGGAAATCCCAGCAGAGGGCTGGGGTCAAAAGTGGTATGG
 TAGTGACGGTGGAGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCATG
 GGCTGCTGGTATCTGACCGAGCTCTATGCTCTCTGGTTATTAGG
 CTCTGTCAGCAGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATA
 TCAGGCAATCCAAGACAAGTCAAGCTACGCTGGAGGAAACCTGAAGGC
 AGCAGCAGGTAGACTGGCTGAAGACAGACAGGCAGGCAACTGTCAATCA
 GATTGTGTTTAAGGACTTTAATCTGGGAGGCCCTCCGGGACAGATCA
 GATGAGAGTGAATGTGCTCCGCCTAGCC
 >Contig37
 GGCGTTCGCAATTCTGAAAGGGAGAGTGGTTTATTATTAAAC
 ATAGTCAGCTGCTAAAGTATATGATATGATAGATAGAGTATAATTAA
 TACTTTCAACTACAGACAAAATCAGGAGAATGGAATTAAAAACAAATTAA
 CAAATGGGTAATGGCAGCATTGGTTGCGCCACCCACGAGAAGGCAGAC

FIG. 3 (33 of 52)

35/118

ACCAAGATTCTAAGATC...ACGTGGCCAGCACCTCAGACTTCAAATAGA...
 TTCTGATTATGCATTATTTCTCGAAAGTTTCACTTCACATATGC
 TACTTGACACTGCTTCTAAGACATCCCTCTATTTGAGATGACTAA
 CTCAGCAATTCAATTCTCACGCATAAGCTGCACTCAACCCAAACCA
 CCAAGCCTGCATTCTACCCCTCAATAAGGTCTGGTGTAAACTGACCC
 CTTCACCTAGTCTTAGCCCTCTTGACCCAGACATGACTCTTCATAA
 GCTAGACCTATAAAGTCAGGGCTCTTAAGTAGCTGATCTGATAGTGC
 AAAGTGTCCCCACTGTTCACATTTCACCTCAGCTCTAACAGGTGATA
 GACTGCTTTGGGGTAGGGGACCAAAACATATAGACCTCATGTTGG
 ATGTAGACACTCCAGTTCTTAATTACAACATATTAAATAATGACT
 TCCAAGTGTACATTTCAGTCAGATCTCCCTGGATCCCAAACCTTGT
 AAAACCCACCCTAGTTGATATCTTGATGTCAGCAGGCATTCAA
 TTTAATACTGTACAAACAAAGTTATTGATTTCATCTGCATCTGTTA
 CAAATTCTACTTGGTAAATAGCACCCAGGCTGTGTCAGTGC
 GAACCTTCCACAGCTCTGGAATAAAATTCAAACATTTCCAAGGCAGA
 AAGGCACAGTGTAACTGGCTCCTGCCTACCTCTCAACCTCGTATCACA
 CTAGTCTCCCTGTCACTCACCCCCCTCCAGGAGCTCAGGTATCCTAAAGT
 TTCTTTCTTTTTTTTTTTTTGAAACAGTTGCTCTGTT
 GCCCAGGCTGGAGTGAAGTGGCATGATCTCAGGTCACTGCAACCTCCGCC
 TCCTGGGTTCAAGTGTATTCTTGCCCTAGCCTCCCAAGTAGCTGCAATT
 ACAGGGCGTGCACCCACACGGGCTAATTGTTGATTAGTAGAGAT
 GGGGTTCAAAITGGCTAAACGGTCTCAAACCTCTGACCTCAAGTG
 ATCTGACCACTCAGCCTCCCAAGGTGCTGGATTACAGGCGTGAACCAT
 TGTACCCCTGCCCTTGAAAGTTCTGATCCAGACTCATTCTGCTTAA
 GGTCTTGCACTTCAAGTCTCCCTCAAATGACACCTCCATGAAGACGCA
 ATTACCTGTAATTACCGTGTCTTTAGTCAATGTGTTGGTTCTGTC
 TCCTCCACTACAGTGTAAAGCTCTATGAAGGCAGAAACCTTGGCAGTCCAG
 TTCCCAAGCACAGTGCCTAGCACACATAGGTATTAATAACACACAGTAA
 ATTACACCTTTAGTGTGCAATTCTGAGTTGACAAATGCAAGTCAT
 TTAAGTCTGACTATTATCAAGCTATAAGATGGTGCAACACTATCACTAA
 TTCCCTCATGCTCCTTGTAGTCAGTCTCACCCCTAACGCCCTCCTG
 GCAATCACTGATCCGTTTTGTCTTATAGTTGGTTCCAGAATG
 CCAATAACTAAAGTTGAATGAATGCTATTAACTCTCATTTCTGAC
 TCCAGAGCAACATCCATGCAATTTCAGGCCAAACTGCC
 CCCTCACCTTCACTCCAACCACCTACTTGATGATAACAGGTGAGACATT
 GGCATGTGCTTCCATGTTCTAGCATTTCCTATCTCCTTAGCCTT
 CCTCTTAATCATAAACGAAGAGTGAACCTCCCTTCTAAAGGCAACTTA
 CTCCTAGGACCTCGATGCCATAATTGTTCTCTAGTACTTCTATATA
 TACACAAACAATTAGCTCCAGAAAGGTAAAGACTCACTGTGCTCATC
 ACTGTGTCTCTAGCGCCTGGCACACTGCAAGGTGCTGAAGAAACACCTAC
 AGAATGAGTGAATGAATCTCTCCCTCTAGACTCCTCTTTGTAAT
 CAAACATGTTCAACCTGCAACACAGTCTTATGACCAATCCTCTGTT
 GACCTAGGCTGAGCTCCAGGGCTGGGACCTGACTTCTTATTACCA
 TCAAGGTCTGCACTCACTCTCTCTGTCAGGATTGTTCTTCT
 TGTCACCAGTCTTCTAGACTTAGGTCTCAGCTCAGACATTGCTGTT
 AAAGTACTTCTACTGATCCTTATCTAAAGCAGCCATTCCAGCCACT
 CTCTGATCATAGCACCCCTGAATTAAAGTGTAACTTACTGTCCTTCAG
 GAGGGCAAGGAGCTGGTGGTGTTCAGGGCTGTACCAAGCTGTACCT
 TGCTTACCCCTGCTACACTTTAGCAACCCTAATTACATGCTCCC
 TTCACCTCGTCAAGAAATTCCCTTATTTCTACTCAAGCAGGTATACATAT
 GTGCTTCTCTGGGAGGCTCACCCACTTCATGAGACTACATTGGTCT
 GGTAGAAAGTGTACAAAATCCACTGGCTCAGTTAATCAATGTATGTTA
 ATATTAACCAACCTGAGATCTTGATTCCACGCCCTGGCTAATTGTT
 TTTAGTAAAACAGGGTTCTCCATGTTGGTCAGGCTGGTCTCGA
 CGACCTCAGGTGATCCGCTCACCTCGGCCCTCCAAAGTGTGCTGG
 GACTACA
 GGCATGAGCCAGCGTGCCTGGCTAAGATCTGATTCTACCATCTGAA
 ACTGTATTGAACTGACTGCTCTGCTGAGCTTACTGGCCAAACTGG
 CCCACTCAGACTCACGGAAGTTCTGGTTCTCCCTGGTAACCTTCTGA
 ACTTAACCACTGGTTGCTTGACAAAGAGATTACCATCTCAGTC
 GCTATGTGAACACTCACTTATCTGCTATTGCTCAGTCAGCACGGCA

FIG. 3 (34 of 52)

36/118

CTTATTGAACGAGTGTCTACATCTGCACCCCTACTTCTTACTCATCCAT
 TCTGTTCAATTCTTAAAAAGAAAAAAAAGCTATTGTAAACATACTG
 ATTACAGAAAATGATTTATAACATGTGTATGTACCACTAGCCCTGTCAA
 GTCTTAATATTGTTATATTGCTTCAAATCTTTTCAGACTGTAGTTA
 AAAATTACTTAGGAGCCATTATTTATGGCTTATTCCTGACCTAGTC
 TTGATGGTCAATTGCTTAATCATCTTAAGTTGCAAAAGCTTAGAATTAA
 AGCAGAAAGTACCTCGATCTCTGCTGTTGCCTCTTTAAATATTGGGT
 TTGTTGGGTCCTTACGGTTGTGACATCAGCTTGAGTTGGGAGCT
 GTCTTGGTCAGAAAATGGTCTGGGGACAGCCTTTCAACTGGAGTC
 CAAAGTCTGTGCTTTGCTGAAAGCATTATTGTTATGTTTATACCAC
 TGGTCCATTGGCTTATGCTAGGGTGCTGGAATGGCTGAATTAAAT
 CTGCCAATGTCAAATTAGGCCTCTGGCTACGGCTTTGACTTTGAG
 TACACATGATGTCTGAGGTATACAAACTGGCTGGACTTCTGATCTGCT
 TGATGTTGGATGTCTGTTATATTACCCCTGAAGCCTACTGGGTAT
 GTTCTGGGTTGGTGTGCTTCACTCTGTTAGTAACAGGGTATGACCG
 TATCTTAGTTCAATTGGCTTCAATTGACTCTATTAAACCTTTATAT
 CTTGATGTTCTGACTACTGGTTCTTGACTGAACTTTACTAAGG
 GTCCGAATAAAGTGAGAGGGAACGGCTCTGAGGGTTACTCTGGTCT
 TGCAAGATCTGCTCTAGAGAGTTGCTGTTGATTTACTGGAAAGTCC
 TGCTTGTGTTCTCAACAAATTGTTATTAAACCTATCTTCAGAAC
 GCACATTAACTGAACCTTGGCCAAGGCTTTAGGAACAAACTGTT
 CTTGGTTGATTAAAGAGTCAGTCTTGGCTTACTCTGGTATATAATT
 TAGGATCTGGCTTCTCAGGTTCTGTTAAGATATCTAGCAAGTTCT
 TTGTTGTTCTTCAATTGAAAGTTATCCAAAGGATTGTTCAACATGGAT
 ATTATTCAAAAGTCTATACATTACATTCTGATCTGTTAAGTCT
 GCTTTGAGTTTCATTGCTCTATTAAGTGACCCCCACAGGTTCT
 GACAGTCCTCTGGTGGACTATCTAGCTTACACTGTTGAAACTCTT
 GCTGAAAAGCTAGACTATGGTTAGAAGAAACACATTGAAAGTCCGCC
 TTTTGGCCAGAAGTTGGCTCTAACCTCAGCTTCTGGGACCCCTGCA
 GTATTAGGTGGCTGGCTGGAGTTAATGCTGATGGACCTTTAGGTT
 GACAGGAAACACATGGTGGTAACATCATTTGGGCTAATAGTCT
 GAAAAAACAAAGAAAATACATATTAAAAAAATCCTAACATATCTTATTGT
 TTTTAAAATAAAACTGTGTTAACACATGCTAAAAAAATCATTTT
 AGAATTTCATCTAAGAAAGTTGAATCCTCAGAAAGTAAAGAAAGACTCAC
 TAATAGGTAGTTTGTTGTTTTTTTTGAGACAGGATC
 TTGCTCTGTCACCCAGTCGGTGTGCACTGATGCAATCTGGCTCATG
 AACCTCTGCCCTCTGGGTGAAGCAATTCTCCCACCCCAACCTCGCAAGT
 GGCTGGACTACAGGCGCATGTCACACCTGGCTACTTTTTGTATTT
 TAGTAAAGTGGGTTTCACCATATTGCCAGGTTGGTCTTGAAATCTG
 ACCTCCAGTGATCCACGCACCTGGCCTCCAAAGTGTGGATAACAGG
 TATGAGCCACACACCTGCTCTAACAGGTAGTTTACAACCTGAGTTCC
 TATCAGAAGTATATTAGAATCTTGTGACAGAAATTGCTCAAACAG
 CAGTGAATATAACAAACTTGCTTTCAAAATGAATTGCTCAAACAG
 TAGTGTGAAATGCCTATTATCTAACAGTGCCTCCAAAGAACCTGAA
 AAAATACATACATAATGAACCTATGTTAGGTACCTCCAACAAATCTCT
 CCTAGTACTTGTATAGCCACACTATATGTTTTAAACCACTGCCTTG
 TAAACATCACAGTATCACTCAAGAACCTCTGCTCATCCCTGGAGATCAG
 TGACAAGGAGATAGGTGGCAGATGATGTGAGGCTGAGATATGCTGCCAC
 AGCTCTCAATAAACATGTAACATCTAACAGTCAATTGTAACATCAGC
 CAGGACAGGGTTAAGGTTAGAGTCTATGTTAATAATAAAACAAATGTT
 AGTCATGTGATTTAAGTTGGATAAGAAAGTAGGACTCGATTACAGAGA
 ATTTGAAAATAGGAAAGGGAGTTAGAATTGATATGGTAAGTAATTGG
 GCAAGCCACTATGAATTCTGAGCATCTCTGAAAGCAATTACTCAGA
 AAGGAGAATTCAACAGAGATTATGGAATATGTTCCAGGGTAAGATATG
 GGAATGCTAGAGTTACCACTCTATTGATTTGACAAATATTGTGAAGA
 ATCACTACATAAAACTTGGCGAGTATGTAAGGATTCTAACAGAACCAT
 TTGGCATTGAGGGCAAAGAAATGTCTACTCTGGATGATAGCGGTGTGT
 GGTGTTACTAGGAGTGAAACAGCGGAGTTGGGAGTGGGAGGCAGAGAGAT
 GGATGGTATAACCCACAATGGCTATATCTGGATTAAATCTTGGAGCACCAAC
 ATTTATACACCTCGGATCTCTCATATTGCTTACTGAAAGAGGTGGAG

FIG. 3 (35 of 52)

37/118

GGACGTTGGCATGAAAGCCTCCAAATGTGTTTTTAGTTCGTTCTTAAT
 ATATTAAAAACGAATTGATATAATCCACAAACCATAAAATTCAACCATT
 AGTAAGTGCACACTCTGGATTAGTATAGCCACACTATTATACAGC
 AATCACCACGTCTAATTCAGAACATATTCAATCACCCCTAGAAAGAGAC
 TTGGGTTACTTGGCAGTCCCTCCCCA

>Contig38

GGTCTACATGTGCTCGAAGATTGGATATTGAAATATCAGCAAGAAATTA
 AAATGACATAGTAGTCATTATGCCTAAATTATTGTTATTTTGATTGAAA
 AAAGTTGAATATTCAAATATCAAGGTAGTAGTGAGATATAATAAGAGA
 GAGTCAGTTCTAAGTATAGAATTGCTGATTCAAGTTAAGCTCTGTTCTCA
 ACATTGGGCCACATTGAAGAGACCATGTAGCTGTTCAAGCCTCGGTT
 CCTCCTTGCAAAATGGGGATTACACTACCTGCCTCACAGAGATGTAAC
 TTATGACATGTTATCATGATTGCCAGGGCCCACCTGTTTCTTAAACA
 TTGAAATCACTGTGCTGAAACAGGGATTCCCTGCCCTTGTGCAAGCT
 CCAGAAAACAGGAGTCAGCTGAGTCCCGCAGCTAAGAACGTGGATTCTGG
 TCATTTCTCATAGCGAACACACTTCACAGGCTTCAAGGGAGTACATT
 TTCCTATAACTCACCTTAACTCAGTTGAAGCCTCGTTCTTAAACA
 CTGTCGCCAAAACAACTAAATCTCATTCTTCACGTAACACTCAGCAATT
 AATAATAGTACAGTCATTATGTTCAACTGAACCAAGTCAGGGTTCCA
 CTCCTGCCTCCCTTCTGCTCTGAGGACATCCATGAAGTGGAGGGGTC
 TATGTAGCCTGGAGCTATTGGTGAGGGGCGATGGGTCGGTGGTCTTG
 GGGAACTGCGGGCTGTGCTGGCTGGTCTGGTCTGGTCTGGTCTGGCCTT
 GTTCCACGCGGTTACGCTGCAGGACAGTTCTGTCCTTCTGTCCTAAT
 GATCAGCTTTAGGCTCACGGGCTGTCTGCTGAGATATGGAATAGGA
 CAGCCCTGGATCTTCTTAAACTCTCCCTGGGCCACAGGGACTCTGTT
 TGTGTCGTGCCCACATAGGATGATTCTGCCAGACCTTGCTGCCATT
 CTTGCTGTTCTGCTGTTTGTAGTCCTGGAGGGCTTGAGTTCTGGG
 GTCCCTGTGGAAGCAAAGCAAAGTCTCTCCACGCTCAGATGTCCTAAACG
 TATCTGGTTTATCGTCACCCATCCCAGAGCTCAGTCTAGAGGAGGGG
 GCAGCCTTCGGGTTCTCCTCCCTCCAGAGCCTTCTCCTTGACCAAG
 GGCAGCCTCTCCATCTGTTGGAAAGGGCTGTCTGGGTTCTGAATATAG
 AGTTGCAAGGTTGAGGGGTGAGGTGAGGTAAGGCAAACATCACATGG
 AATAAAAATTACCCGTGTCAGGAACAACCAGAGCTGGACAGTTTAA
 ATGTGAAAACCAATTATTATTAGGACTATGGCGAGAGGTGAAGTAAGACC
 TCAGTATAGAACTGGGCTCAATTCCGAATGCACTGGGAAATGGGAAAT
 GTATAGCCTAGGAGCAGGGTGGGAAACCTGTGGATGAAGAATTACTAAAAG
 GGCATATCAGGGTGGGGCTCTGGCTACACCCACTAACTACTGTT
 GCTGAAGAAAGGCTGGTACATCACTGGGAATGGTGGGGATGAAGAA
 TCCAAATCAGATGGATTAGGAGATAAGGGGATCTTGATAAAACTGGCTTAG
 GAGGGTTTGTCTAAACTGGTTTCAAGGTAAGTCCACAGACAGGTCT
 TGGAGAAAGTTCAGGGACCTACGGTTGTCGGGCTAGATGCTTGTCTAC
 TGTCACACTGGCACTGTCACCTGGCTTCTTCTGCTCCCTCCCCCTT
 TTTTTCTGGAGTAGTTGGAGACCAAGAGGGAGCTGGAGTTAGGGAG
 AGTAGTCAGAAAAGGCCAGAGAAAATAAGGAGGTGCTGTAGGGAAAATC
 CTTAAATCCTCTAAATTAAATTAAATTAAATTAAATTCTGGGACAAGGTC
 TCACTCTGTTGCCAGGCTGAAGTGCAGTGGTGTGATCTGGCTCACTGC
 AGCCTCGACCTCAGGGCTCAAGCAGTTGGCCACCTCAGCCTCTGAGTA
 GCTGGGCTCACAGGTGTCACCATGCCGGTAATTGGTT
 TTTTTTTTTTTTTTTTTTTTTTTGTAGAGATGAGGTTTGCCTAG
 TTGCCCAGGCTGGTCTCGAACCTCTAACAGTCAGGATCCACGTCGACCTC
 CCAAAGTGCAGGATTACAGGCATGAGCCACTGTGCCGGCTAAATTCT
 CCAATTAAATGCTCCCTGTTCCCTGTTCCAGATTGGGATATTGAC
 TGCTGTTAAATCAGCGATTCTCCCTGTTGGAGAGGTAGCCAATAGGAAGC
 AACAAAGAGTGAGGAGTCCTTATATCGAAATAGGGTAAGAGAAGAGACA
 GATGTTATCTGGCAGTGTGTTAAAGAACAGCGAGTGTAGCAAGCAAAGC
 AGCAAGGCTCCAGGTGCTGAGAACAAATGGCTTCTGGGAAGCGTCTG
 TGTTCAAGAACCTTAAGTGGAAACATCTGAGATGTTGCCATGAAGG
 TTTCTCTGAAGTGTGAGTCTTCATCACTAGGTAGGCGTGTGGAGT
 CTCTATCAAACAGATCCTGTGTTATTAGGAAGCTGTGGTCTAAAGCC
 CCATGCTAATTTCAGGTAGCAGGGTGGCCCTGGCCTGACCCGGGACA

FIG. 3 (36 of 52)

38/18

GAGTGGCTGCTCCC...CAGGCAGGAAACTCTCTCCTGCCACCTAGT...
 CTGCATACCCACATTCAAGGGAGCTCTGGGTGGTAGTTACCAAGACT
 ATGGTCTGAGGTAGAGTAAGCAAACAAAACAAACTAAACTGCATAAAGAAAC
 AGAAAGAAAATCAGGTGTTAAAAACAAATTGGCATTTGTTGTGTT
 AGCTCCGTGTCGATTTATTGCTTCCACAAATAGTGCGATATGCACCAGG
 CACTGTTGAAAACGTAAAATGTTTGATGTGCCAGTCTGTGAGT
 ATTAAACGATGGTTGATTGAAATTGCTATGATTCATATTCTGGGGGT
 AAGATGCAGGATTCTTGGGGGCCTACGATGTGGCATTCTAGAATTCT
 CAAAGAACATCAACCCCTGGTGGGACCAAGGAAGAGCTGAGCTGAGGCCTCT
 GCTCATGTGACTTACTGGAGATCATGGAGACAGGTGAGCCTGAGTGCAC
 GTCTCACCAAGCCACAGCAGAGGGGAGGAGGCGGAAAGAGAGCTCT
 CCATTTCTGAGAAGTTAATGTTAACATGGCATACATACCTACTTACAG
 TTGAAAATTGAAACACAGCATTAAAGTGTTCATGAAATTGGCAATT
 TGGGAGTTTCTGAGCTGCATTGGATGTGGTTTGATGCTGTAGGATG
 AGCAAGAGATGATGGAGAACATCTCCTTTGAGCTTCCTTGGACGTG
 GGTCACTCCCACTCATGGAATTAGAAAGCTTAGACCTAGACTTGAATCTC
 ACCTTCTCAAGGTGCTCCGGGCAAATCACTTAAGATCCATCTTCTC
 CTCCGCTCCCTCTCCCTCTGAGTTTTTTCTTCCAAAATT
 AAATGACACGGTACTGGTAGAAGAAAAGGTCCAAGTCTGCTTTACAGCT
 CCCCTCATCCCCAAATGTAAGTCCGACCCCAAGATGACCATGTTATCATTT
 GATTGACATCCTCTAGTTCAACTCATTTCTTGATGTTATGACGT
 ACATATAACACTATTTATTTGCCAGGGTCACCGTTAGCTGCATTAAT
 TTCTTATAAAATAATCTATTTACTTATGGTTACGTAAAACAACATAC
 ACATGTAAGTGTATAGCTTGATAAGTCTCACTGTAACCAAAATAAAA
 TTGGAAGCCCCCAACCGTCTGAATGGACCCCTTCTTGGCAAGAGC
 ATTCCAAAGTTAACCTGAAAAAAACTAGTTCAAGGTATGATGGAGGGAG
 GTTGGACATGCCCACTGATACCCCTCTCCCTTGGAAATTGAGAAAAGC
 TGACCAGCATTAACATCAACACAGACCTTATGCTGATAGGAAACTTGA
 CAATCTATTCCCTCTGAAGCTTGTACCCGGAGGCTCATCTACAAGATA
 AACACCTGGCTCCACAACCGCTTATCATAAACCCAGACATTCTTCTG
 TGAGAATAATTACCTTGTAACCTGGAAGCTCCCTGCTCAAGTTCC
 ACCTTCCAGATTGAAACCAATGTAACACCTTACATGCAATTGATTGATG
 TATGTCCTCTAAGATGAAATAAAAGCAAGCTGATGTTGACTGCCCTCAG
 CACAGGTTGTCAAGGACCTCTGAGGCTGGGTACGGATGCATCTTAACC
 TTGGCAAAATAAAACTGTCTAGATTGACTGAGACCTATCTCAGATACTG
 GGGTTCAAAATAAACTTATGAAACTAATACACAAATCAAGTCATAGAA
 TATTTCATCACTCTCATCTACCCCCAAATTCTTCTTATGCGTCTTGCA
 GTCAACCTCCACCCCATCCCCAGGCAACTGCAGATCTACTTTTGTCTC
 TGACCTTCAACTGACCCCTTCTGTGATTCTATGAAATGGAATCATGCG
 CTGAGCAGTCTTGTGCTGGCTTCTTGTGCTCAGATAATGTTTTGA
 GGTTTGTCCATGTTTGTGTTGCAATGGTAATTCTCTCATTGCA
 GAGTAGTTTCTATTGTACATGTTGACCAAAATTGTATATCCATTCCAT
 TGCTGATGGACATTGATTGTTCCAGATTGGCAATTATGAAATAGAG
 CTACCATGAAACCCAGGTACAAGTCTTGTGTTGACTTATGTTTCA
 TCTCTGGAAATGAACTGTCAATCAATAAGTATATGTTAACCTTGTAA
 GAAACTGACAACAAATTATGCGATGGTTATGCCATTGTTTCTAC
 CAGCAATACACGAGCATTCACTGAGCTCCACAACATTGCCAAACTTGT
 TTCTTTAATTGGACATTAAAGTGGTGTACAGAGGCACTCATGTTGGTT
 CTAGTTTCTTGGCCCTGATGACCAATGGTGTGAAACATCTTCTATG
 CTTTTGACCATTTACATATCCTCTTGTGAGTGTCTGTTCAAATATT
 TTTGCCATTAAACATTGGGGTTTGTCTTATTATTGTTGTTGGGAGA
 GTTCCATATTATTATTGAGATGGAGTCTCAGCTGTTGCCAGG
 CTAGAGTGCAGTGGCGTACCTGGCTACTGCAACCTCCACTCCTGG
 TTCAAGCAATTCTCTGCCCTAGGCTCTGAGTAGCTGGGATTACAGGCA
 TGTGCCACCAACTGGCTAAAGTTTGTATTAGTAGAGATGGGGTT
 CATCATGTTGGCCAGACTGGCGAAATTCTGACCTCAAGCAATCCACC
 TGCCCTGGCCCTACAAAGTGTGGATTACAAGCATGAGCCACTGTG
 GCCCATATTATTCTTATTGTTATTTGTATACAAGTTCTGTTGAG
 ATACAATAACCTGGTCAGATGAGATAATGAGTTGAAAATGCTTGCA
 AATGGGGAGAATAATTAAATGTTATTATTAAGAGCAGAGGCC

TTCTGTTGGTCAC...AAGCCCTTGCTTCTGCCTTTATAAA...
 AGCAGAGTCGAGCTACACAGGCTGCTGTGGCTGCTATTAGTTAAC
 AGAGAGTTTTTTCTTCTGCCTGTCATTCTAATTGTGACACATAATT
 AGCCACAATATGTGTTTCAGTTGTGACACTGGCTGGAAACCAAGGG
 TGTTTAGAGTGGATTCCTTGATTTGCAATAATTGTGTTCTGCA
 TCTTCTGTTAACACAAATTCTGGAAAGCAAACATGGAAAGCAAAGTACC
 CTGGACATCCCCCTTCTTATGAAATTGATTCTCTTAAATGTAATGTT
 TGCTTGTCCCTTACTTTAAAGCAATTAAAGAGTTATTGAGAAAGTGA
 GCCCTGGAAACATAGATGCATAGAGAGAAAATTCTACCACCCCTCAGGTCC
 CTATTGTCTCTCTCATAAAGTAGTTCAAGGGCTTTAGAAGTTCT
 TTTCTGCTGATTGCATGTTGTGAGTGTGCTATTAAAGTATTG
 ATTTGGTCTGCAAATCTATGAGAGATGGCAACAGAGTAGGGATCTCAA
 GCCTGCAGGTGTATTAAAGTCCAGCAGGGCCTGTATTACAACAGAGGG
 TCCTGAAGACATTCCATATATTATGCTAGGGAGTGGCCAAGCAAAC
 TAATGTGTCCCTATGGTGGGATAATTGGGGTTAACCTGCCCTCTCTT
 AATTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTGAAA
 TGTAGTCTTGTCTTCACCCANGCTGGATTGGAGTGCAGTGGTATGATC
 TCAGCTCACTGCAACCTCCACCTCTGGTTCAAGCAATTCTCCTGCCTC
 AGCCTCCCAAGTAGCTGGACTATAGGCACACACCACATGCCTGGCTAG
 TTTTTTTTTTTTGAAACNGAATCTCGCTGTGCGCCAGGCGGG
 CTGCGGACTGCACTGGCGCAATCTCGG

>Contig 39

CGCTCGCATCCCTCATATCCATGAGTGTCTGTGGGCCCTGCCTCTGAAA
 TAAATCTGCCTTGTCTCCAGTTCACTCCAGCCACCCATCTGGGCT
 GCACCCCTCCCTCCCTCCAAGCCCTCTCCCTTCTGGTGTGCTGT
 CATGTCAGCATATGCATCAGTGGCACCAGGACATTGAAATGCAACAG
 TACAATTGGCGCGGTATGCCTACCAGTTTCTTCTTAAACATTAA
 TATTATGTTGAAAGCATGCCACTTCTTCACTTGCCAATTGACAGA
 TTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGTTAATTGTT
 TTTGACATGTAGCTTAATTCTCATTATCATTATAGGAGTTATTC
 TTTGTAAGGGTAACTGAGTTCTAAACAGAAAATTGGGGTGG
 CCCATGGAGCGTGACTCATGAAATCAGATTCTAGAAGGACCTCGGCAAG
 TCTCTGGTTGCTGTTATGAGCCTGGCTGGCTGCCAGGGTGTCTGC
 CCTTATGAGGCCACCACTGTTCAAATGCTGCCTGCAGCATTACTGCC
 TAGGTAGTGTGTTCTACTGAACCTGTCAAGGATCCAATTCTTGTGGT
 CTAAGTAACAATCTCAGATTACAAGGAATTGATTAATAAGCCAGAATG
 CCAATGTATTACATTGATGAAGACCAATTACAGTGTATTCTGC
 CTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATGTGAGAAGT
 ATGAGGTTAAATACATTGAAATTGGACTTTCTAGAAAATCTGAATGTGA
 TTGCCATTACATACCTTCTGGGGATGATGATTCTGTACTTTATT
 AAAAGACATAGAAAACACTTAAGAATCAGATTGCTTGGCTGGCACAG
 TGGCTCATGCCGTAAATGCCAGCACTTGGGAGGCCAGGTGAGTGGATT
 GCTTGAGCTCAGGAGTTGAGATCAGCCTGGCAACATGGTGAATCCCA
 TCTCTACCAAAACACAAAAAAACACACACACACACACACAC
 TTAGCTAGGTGTGATGGTGCCTGCTGTAGTTCCAGCTACTGGGAGGAT
 GAGGTGGAAGAATTGCTTGAGGCCAGGAGGTGGAGGTTCACTGAGCTGG
 GGTTGCAACAGTGTACTCCAGCCTGGCGATAGAGTGGAGACTCCGTCTCA
 AAAAAAAAAAAATCAGATTGTTATTGCTGGTTCTTCTAAACTGA
 GATTGGGTCACATCCCCTGGCCCCATTGGTTAATGGTCTCCTT
 GTCTATTGAATAAAATACAGATGTCTGTTGGCAACATGGTGAATGT
 AGACACTGCAGGGTCTCCTGACTAAATGAGTAAGGCTTAGATAAAAC
 ACATTTGAAATGCATTCTGGATGAACAGCAAGGAAGGAGATCTCTTA
 AAATCCTCTTCTGTTCCCCTCCCTACCCCTCCAAGTGGCTTAAGT
 AGGAAGGGTGGTGGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTTCTC
 TCTGAGGGAAAACACTGTATAAGCATTGCAATCAATGGGCCTTTAAT
 TATGTGCCAGTGGCAAGAGCGGGTGTGAACCCAGGGGCTGCCCTCAATC
 CGGGGCCTTGAGGCAGAATAAAGTGGTCTCAGGTTGGCATTCT
 GCCCTCCACCGAAGCAGACACAAATCTCTGGAGGCAAGTCCCCA
 ATTCAAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAGCTCA
 CAGACAAAGGTACCAAAACACACAGAGCAATAACAAATTGAGTGAC

FIG. 3 (38 of 52)

40/118

STGAATGAGAATAAACAC...AACAAATAACCACCAGCTGGGATGCTCTAAG...
 CTTCAGCTTCTAGAATTCTGAATATAGAATAAAAATGCCACAATGGCAA
 ACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTCACATT
 GTGCCAGATACCGACTCAGCTTCACACTCACCCCTCTACTGTGCCCTCTT
 AATTTCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTGTTCT
 TGGCTGTGCCCTTGGCAGCACATGCAAAATGGGAGCTAACAGTGGCAGTC
 ACAGGTAAAGTAGCCTCTCACAGTGTGGAGTAAAGGCATGGGACTGAGA
 CGAGCAAGGTTCTAAAGGGACAGTGGCAGTAGATGACCAGGGGCTACT
 GGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTGGGCTTGCA
 GGTGCAAGTAGCAGCTTCTGTAGTCTCTGATCTCTGGGCTCCACAATCTT
 CCCCGTTTGTCTCTCACTTCTAATTTCAGTAACTGACTTCCCTGTGTG
 TACTTCTCTCTGATTGAAATAGCCAGACTGGTTCTGTTCTGATAA
 GACATTGTCTGGTACGAACACAGTAACCTATTAAATCCGATATCTCTATG
 AAGGAGGTACAATAATTATTCCTATTACAGATGAGGAAACACAGCAGA
 GAAATAAAGTCAATTGTCTAAGGTTGCACATTAGTCAGGGAAAGGGTTG
 ATATAACATATAATTATTTAGAAAACATCTAAGGAAATAAAGGCATAAT
 TTAAAAATAAAACTAGGCAGGTTAAAAAAATGAAGTAATCTATAAGTAA
 AAAAGTATAATTGTTGAAATACATACTTAGTGGATGGGTTAAATAGCTG
 AAGAAATGATTAATGAACTGGAAGGTAGTCTGAGGAAATCAGAATTCA
 CATAGATAGAAAAAAATGGAATTACAAAAGTACACAGGAATTATAAAAG
 AGGTTAAATTATAGGGAGGGTAGAATGAGAATTAAACATTGGCTAACTGG
 AATTGGAGAAGAGAAATAGAGAGAATGAACAAGGCAATATTAAAGAG
 GTGGCTGAGAATTTCAGAACCAACACAAACTATGACTTACCAAGTGA
 GAAAACAATGTACACTGAGGAGGATAAATAATACATATGAAACAATTG
 TAATAATAACTCAACAAAGACAAAGAGAAGATGTTAAATCAGCAAA
 AAAGAAAGTCAGACTAGAAAGAAATGACAATGGCAGACTACTCAACAAAC
 AACATGGAATCCAAATTGGTCAAACAGTATTCTCATGCTAGCATA
 TAGC

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GGGAGTCCGCTATGCTCTAAAGATTGACCTCTGATCTGGTTGTAGT
 TAGTCTCTTTATTGCTTATCCTACTCAACTAATTTCAGTGCCTGT
 TTTTTTTTTTAATGTGTGTTGACTACAATTCTAAACTCATTCTA
 CTGATTCTGGGTGCTTAAAATCTGAGCAGTCTTCGCATTACTGCCT
 GTGATGGCCCCTCCACCAAGCTAAAGTGTGGCCACTGCTTACAGCACC
 ATGTGATAACGAGTAAGGGAGAGATGCCGCCAGACTCTCTAGGAGCAG
 CCAGTAGGACCTTCCAGGGGTTGCAAGCAAACACAGCAATATGTGGAGT
 GTGGCAGAGGATGGCCCCAAGAGGATGTGGCAGCGGCTAGTGCAGCTCAG
 CTTAGTCTGAGAGGAATGCTGGAGAGGAGAGGCCAGTCTGTACAGGCAT
 GACAGCCACAAGGACTTCAACAGCTAACATGGCTGAGTGGACTTTATGTG
 CTATCTCATTCAGAAAACAGGAGCAATCAGAAAGGAGTCACCTCCTATT
 GTACCCCAGGAATTGCTAACCTACTTGCTATGAAATGATGTCCATCACTT
 CCCTCATCACCTCTGGGGCTCTGCAAGGATTGACTCCTGCATTA
 GTGATCTGTCTCACCTACGTTGATTACATGAACTACTAATGTGCTA
 TGTGACAACCTACCATCTAAACACAAAACCCCTTTGATTCTGTGGCT
 CCCTCCAGCTACCCCTGCATTCTGTCCCCCTGCCCGTCTGCAC
 CACTTTATTACAGCAAAACTACTCAAGGGAGTCTCAGTGCCTTGG
 CTCCATGTCTCACCTTCATTCTCTCAGTCAGTCCTGTCAAGGCTT
 CCGTCCTCAAGCTCTTCACTTTGTTCTAGGGCCGCTGACATCCTCT
 TTCTGCCAAATTCACTGGCCAGGTCTCACCTACTCAACTGCTCAGCAT
 TGTTGGGCTGGTGGACACATTCTCCTTCACTGGGACTCCTCTTGTCTC
 TCTCTCTCCAGATGTTCTCTTCACTGGCTACTCCTCTTTGTCT
 CCTTGTTAGCTCATTCTTCCAACTCACTGTGCTGGTGTGCC
 AGTGCTCAGTTTAGCTATTCTCTTCCAGTGGCATTCAATTAGATG
 GTATCATGTGACCCATGGCATTATATGCCCTCTACATGACAGTTACTCCT
 GAATATGAATCTCAGGAAAGATTGGATTATTTAATTAAATTTTTA
 AATTAAATTAAATAAAATGAGGTCTCTCTGTCACTCAGGCTGGAGTGT
 AGTATTGAGTGTGATTATAGCTCACTGAGCCTTGAACCATGGGCTC
 AAGTGATCCTCCTGCCCTAGCTCTGAGTAGCTGGGACTACAGGCATGT
 GCCACCATGCCCTGGATGACTTTGTGTGTGTGTGGAGACAG
 GGTCTTGTCTATTGCCAGGCTGATCACAAACTCCTGCCCTCAAGTGT

FIG. 3 (39 of 52)

41/118

CCTCTCACCTCAGCCTCAAAGTGTGGATTACAGGTGTGAGACCA
 CTGGGCTAAGATTCAAGATTTGTATTCAATTGACTGTTGACATCTCAC
 TTGGACACCTAACAGAGGTATCTCAAATAATTAAACTGGCCAAATACA
 GAACCTTTGACCCCTGCCCAACAAATACTGCCCCCTTCCCAGACTTC
 CATTCTGTAAATATCCCCAGTTACTCAACCCCTCAAACCTATGAATGCC
 CTTTGATTCTTCTTCCCTCATCTCACGTTGACGCCATCAGCTAGT
 TTTGTTGCCTTATGCCAGAATAATCCTCACACCTCTCTCTCTTAT-
 GCCAGTATAAGATGTCAGTTCTGCACAGTCCATTGCCCTGACCT
 CCTGAGTGGTTGCTTCACTTTGACATTGTATTCTCTTCCCCAG
 GGTCAATTTCACAGCAAGAGTGGCATTTTTTTTTTTTTTTG
 AGACGGAGTCTCGCTGTCCCCAGGCCGACTGCCGACTGCCAGTGGCG
 CAATCTCGCTCACTGCAAGCTCCGCCTCCGGGTTCACGCCATTCTCT
 GCCTCAGCCTCCCGAGTAGCTGGAAATACAGGGGCCGCCACCAGCGCCCG
 GCTAATTCTTGTATTAGTAGAGACGGGTTACCTTGTAGCCAG
 GATGGTCTCGATCTCCTGACCTCATGATCCACCCGCCCTGGCCTCCAAA
 GTGCTGGGATTACAGGCGTGAGCCACCGCGCCGGCAAGAGTGGCATT
 TTAAACCATATATTAGATCATGCTTTGTGTTGGAACCTCCAAGGG
 CTTGCATCATATCAAGTTGACACCTCTCCTACCCAGCCTGGCTT
 TCCTGCTCCTCTGTCCTCTCAGCCCCCTCACCCATTGTCATGCTGCTTC
 AGCCACACTGGCCTCTGCCATGCCACATTGTGCTAACGCCACATCCA
 ATCTGGGCCCTTGCACTCGCATTCCTGCTTGGCATGCTGTACCC
 AGATCTTCATGATTGGCAGCTCTGTACATTAGCCACCTGCTCAAGCC
 ACCCTTCAGAGGGCCTCCCTGGCACCTCACCTGAAATAGCACCTCCG
 ATTGCACCCATCCGGTATTCTCATCCTGTTCTTGTGTTGGGATTT
 CCATCACTGATGAGGAATGAACCATGGAATGCTAGGGCTGATGACCAGA
 ACTTCCCCCACCCCCACATTATACAGAGGAGGAATGAGGTGGAGGT
 AAGATGGGCCAGGATTCTACTCCGCCCTGGACTGCAGGCACAGCACTG
 ACCTCAGCTGTGCTCACTCTGGCATTCACCCACCCCTATCTCAAC
 TGCCCCATTACAGAAAGTGAATGTTCTAGAGACGGTGAGCCACCTG
 ACTTGGACAGCAGCCCAGGGCCCTGGCACCTGCTTCTCCCTGC
 CATCCTTCCTCTCCAAGACCTACCTTCCCTGTGATTCTGCCACATG
 CTGCATTTCATGGTTTATGACCTGATTCTGAGAGGGATTGAATTT
 ATGATTATTATGTAAGCAAATCATTATGCTTATACAAATGAGAAAAGGA
 GTGCTTCTGGACTTCCAGGGACAAATCTGCACTTGGCTTGTCA
 TATTGCTAATTAAAGGACCCAGGATGTGGGTGAGATGTGCTAAAGCTGAG
 AGGAGGCTCTGGACTCTGACTATGGGCCACACCCCTGGGAGGCATCAC
 ACTAGCTTCTTAGGTCTACCTCAACCCAGCTTCCAGTTGAATCAGATGTT
 TGTGAATAACTCAGCAAGGCTGTATGGGAATGAAGAATGAGGTGGGAA
 GAGGCCCTGTGAGAAGACACACTGACTTACCCCTCACCTTAACCTAGGG
 TGTGTAGGCCACCCACCCACCAAGTCTGCTTCCAGACCACCGTATGC
 TTTCTCCACCTTGCACTTTATCTTCTGCCAGCCAGATGCTGCTG
 ACTCCAGCCAAAGCCTATAGGATAAGCTACAGCCTGCCCTACAGACTAC
 GCATTGAGAATCTAAGACATCAAGTCAAGTCTGGAAAGCAGCTGCTTCT
 CCTCTCCAGGTACACAGGCTCTCTGGAAAGCTGGTAGCAGCTGTGGAGG
 TGTGGTGTGTACCTGCTGCAGGTGAGAGAAGTTGACTTCACAGCCCTT
 CAGAAAGACTGCCCTCTCAGTTGTATTGTGTACTTGGCTTGGGTGTGG
 GGAGGATTCTCAGCTTCTCCACTCAAATTATCAGACCCCTTCCATTAG
 TGGTAGACCATTCCCTCGTCCAGGCCAGGGCACATAGTACAGAGAAAT
 AGGGAGTTGTACCCAGGGAGAGAACTTGGCTCTAAACCTGTAATAGAAA
 GGTCAAGTTCTGGCTGGAGGGTCAATTGATCTTGGCTCAGATCCAGG
 AATTGGAACCAAGGCTTTGAACATTAAATGCAAGGGGATTAAAAAAATG
 ATACGAGTCATTCAAGAATATATTGCTTAACATCTAAAGAGATCCCTCA
 AACACTAGAAAAATAAGAACAAAATCTAATAAAACAAAATTGTTAA
 ACACATTACCAAATTCTGGTAAAATTCAAATGTCATAAATA
 AAGCTAAAGTCTCTTGATGACTCGCTCCCTGCCCTATTCACTCCAA
 GTAACCACTATTATCAGTCTGCCAATACCCCTCCAGACCTCTACCTC
 TATATACCATAGAACGACATGGTTTGCAATTGAGGATGTGAGTGT
 GTTTACGTAATGTTATCACTCTGTTCTTCCATAATTGCTTCTT
 CTCTCAATGATTGCTTGGCTATCTTCTATTTCAGTAGCATCTCCTTTC
 TTTTAACCTACCATGTTATTAAACCTTGCCTATCAACAGATATGT

FIG. 3 (40 of 52)

42/118

AGGTGTTCTAGTTGA TTCAAGTATTATAAAACACGCATCAGTA
 GATGCCATAAATTCTTACGGAAGATGGCAAGTAGTGGATTGCTGAG
 CCAAAGAACATGTTAAAAACCCAAAAACTAGACGCTACCAATTTC
 TCTCAAAATGGCCATACCCACTTACCCATACAGAGATGATTGGAATCT
 GGCTCCTCACAGGTGAGATGCCCTCACAGTTCATCTCTGGCATG
 TCTTCCCTTGTATCTGAGAGAGCTGGCAGAATTGTCACAAATCAA
 GGATAGAGGGTCAAATGACAGCTCAAGCTCACAGGCACCTCTGCTTCTT
 CCCAGACCACCTGCTTCTGCCACCAGCTGTTCCATCTTATAGAATG
 GTGCCACTGGGTGTCGCTCCAGCCATGTCATCCTTGACTGCA
 GTTATGAAGCAGACAGAGCTAGGAGAGGGCTTGCCAGCCTCTGCCCTA
 GCTTGGAGAATTCAAAGAAGGAGGGTATTGAGAGTGAGCTGCCAGAC
 TGGCAGCTCCCTCAACTAACAGTTGTCCTCCAAGAACAGTCAGATACA
 TTTTTTGGATAAAATATTAAAAATTATTATTATCTGAATAATA
 TATTACATGATTCAAACACTGTAGGCCAGGCATGGCTGCTTATG
 CCTGTAATCCTAGCAATTAGGAGGCCAGGGAGGATCACCTCAGCC
 CAGGAGTTCAAGACCAGCCTGGTAACATAGTGAGACCCCTGATCTACAA
 AAATTAAAACAAAATTAGTGGCATGGTGGCTGATATGGTTGGCT
 CTGTGACCAACTCAAACCTCATGTTGAATTAAATCCTCAATGTTGAGG
 GAGGGCTCTGGTGGAGGTGATTGGATCATGGGGTGGTTCTCCCTTGC
 TGTTCTCATGATAGTGAGTGAGTTCTACAAGACCTGGTATTGAAAGT
 GTGAGCACCCCCCTCACTCTCACTCTGCTCCGCATAGTAA
 GATGTGTTGTTCCCCCTTGCCTCCGCATGATTGAAAGTTCTGAA
 GCCTCCCAGCTATGCTTCTGTACAGCCTGAGAACTGTGAATCAGTTAG
 ACCTCTTTCTTCATAAATTACCCAGTCTCAGGTCACTTTATAGCAGT
 GTGAGAGTGGATGAATATAGTGCATATGTTGATTCCAGCTACCCAG
 GAGGCTGAGGTAAAGAGGATTGCTTGAGCTGGAGTTAAGGCTGCAGTG
 AGCCATGACTGTACCACTGCTCTCAGCCTGGTGACAGCGAGACCTTGT
 CTCCAAAAAAACCAAACGTGTAATGTGTCATAAAAGTGT
 TTGCTCCACACCTGTCCTATATCTTATTCTCAGCCTCCGACA
 ACTTTATTCAATTCTTATGTATCTCAGAATCAAACAAAATCAA
 TACAAGCACAGTGAATGTATTGCCCTCTCCCCCTCCCTTGTACAT
 CAGAGTTAGCATATCATAAATACGGTCTGCATTTCAGCTA
 TCAGCATGTTGGAGAGGATTTCATATTCTGTCAGACAGCATGTATTAG
 TCAGTCCTGCTTGCTATAAGGAAATACCTGAGACTGCATAATTATAA
 AGAAAAGAGGTTAATTGGCTCACAGCTCGCAGGCTGTTCCACAGGAAG
 CATGGCAGCATCTGCTCTGGGGAGGCCTAGGAAGCTTTACTCATGCA
 GAAGACAAAGGGAGTGGATGCTTATATGGCAGGAGCAGGACTGAGAG
 AGAGAGAGAGAGAGAAAGGATGCCACATACTTTAAACAACCAGATCT
 TGTTGGAACTCTGTCAGGAGAACAGCACAAAGGGATAGTGCTAAACCAT
 TCATAAGAACCTCCACCCCCATGATCCAATCACCCCCACACCAGGCCCCACC
 TCCAACATCGGGATTACAATTGACATGAGATTGGCTGGACACAGA
 ACCAAACAATACAGAGTGCTTCTCATTCTTCTATAGCTGCCTAGTA
 TTCTATGTCCTTACTTCATTAGGAGCTCTGTTGATAGACACTTGG
 GTTACTTCAATTCTCATTACAATGATGTGCAATGAATAATTGAA
 TCATTTCACATGGGTTATGTCATCTGTTGAGATAAATCTCCAG
 GAGTGAATTGCTGGATCAAAGGGGAAGTGCACTTGTGATTTCATAGTT
 AGCAAATTGGTCTATAAGGTCTATCAATTATAGTCCCACCGCTAA
 TATTAACAGTGGGATTCCGACAGTTGACCAACAAGGTCTGTTGAGG
 AACCTTTGATTTGTCATCTGATGGAAAATACTAGTATCTCAAAGT
 GCTTTAATTGACTTCTTATTACAATGTTAAGCATCTTACTCTGC
 CCAAGATCAAATAGTATTCTTCTGTAACAGACTGTTAAGATCCCT
 TGCCCTTGTGTTGCTGGATTGGTCTTCTCAAATGTTGAGG
 CAGTTCTTACATGTGAAACAAGTTATCTCTTATCTGGGTGAGTTA
 CAACTACTTTCTCTGGCTGTTGCGCTTGTACTTGTCTCTGGTGA
 TTCCCGCAATTCTGAAAGTGTACTTTGCACTCATTCTTATACACC
 CATGCTCTGTTCACGCTGGTCTACCTGAGGGCTTTCTTCTG
 CTTCTATCTGGGACATTTTGAGAGAGAGTCTCACTCTCGCCAG
 GCTGGAGTAGTGCAATGGCGCAGTCTAGCTCACTGCAACCTCACCTCC
 TGGGTTCAAGCAATTCTCTGCCAGCCTCCAAAGTAGCTGGGATTACA
 GGAGCCCCACCAACCAAGCCAGCTAATTGTTGATTATTATT

FIG. 3 (41 of 52)

43/118

TGTAGAGATGGGAGTC...ACTATGTTGCCAGGCTGGTCTTGAAGCTCC...
 GGCTCAAGCGATCCACCCACCTCGGCACCAAAGTGCCTGGATTACAGG
 CGTAAGCCACCATGCCAGCCCAGTGTGGAAATCTCTGTTATCCCTT
 TAGGCTTATTCTATGTCGTTCTCCCTCCTCTGGATACTCCCTCT
 TGTTCTTATCTTACTCTACTTGTATGTTACCTTGTCTGCTTATAAC
 TAGCTGCCCTCCTATCTGAGGAGGGACTTGTGACTGTTCTCATCTGT
 ACTCCCAGCTCCTAGTACATAGCGCTTGCTAACAGATGTTGGTGCATT
 GATAGATAAAATCACTGGTAGCTTACTACCAGTCCTGACTCCCTGCAGT
 GCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCCTCTGTTGAAC
 AACAGAAAATAAGGGATGGGTGAGGAGGATAGTCTTCGGTGGCCAAGGA
 TATTTTAAAGGTTAGGACTTGCAGCACTCAGCAATGAGGAGTGGGTTAGTCC
 CCCAAGAACTCTCACAGCCCTGGGTGTTACTGTTAGTGTCAAATCC
 AAGACAAGTCAATGATCAGGAAAGACCATTTTTTGTTAGTGAAGT
 TATTTCAGAATCATTGAAACAGTATGATATTGGTAATTCTATAAATATT
 CCACTTAAATGATCGGAGCAGATATATTTCAGTCGTAATTAAAGGACA
 TGATTAAAGAGAGCACACCAGTCAAATTGAAATGATTCCATAGCTATT
 AAAAAAACTAGGGTTTTTACAGACAATGATACTTTTGGCCCCCTTGAAT
 AGATTAGACCAATGAATAAAACAAACAAATAAAATAAAATAATAGGG
 AAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTTCTTAGA
 ACCAAATGTGCCGTGGTTCTGTCAAGCGTGCTTAAGTGAGTAGGAGA
 GGTGAGAGAGGGCTGGCTCAACAAAAGGGCTGGGATGTCCCTGAAGAA
 CCAGAGCTGANTNCATCAGGAGTAACANAGGTAGATAG
>Contig 41
 CCGCGTTGAGGTTCCACGCAGTTCAAATTATGTCACATTATCAACATTAA
 TGACACATTTCATAGAACCTGTTCCGGTTTCTTAGGAGGGGGGGGG
 GAGACGTTCTCTGGGAATAAGTGTACGCAGGAGGCTGAGAAGGCTTC
 ATTCCATAGCATTCACTTACCTCAGCTGTAGAGTGGGTTATCATCTT
 CAACACGCAGGACAGGTACAGATTTTTCTTGAGGCCAACGCCAG
 GTATTTCAGTCAATTACTTCTCTCCCTGTACAAAGGACATGGAGAACACC
 ACTGAAGAAAAGAGGGGCTTGTGGTTAGGGACACAGCAGTGCAGGGTC
 ACCCCAAACCCCTAGGCCCATGAGTAGGATACATGTAATTGGTAGCCTC
 TGTGGGAACCCACAGTGTAGGTTCTGGCTAAGACACAGGATAACTGA
 CTTCACAGACAATAGCAGGGTCATTGGTGAATTAGGGTTCCCTC
 AAAGGCCCTGAGGGTTCTAGAGCCTCATAGCAGTAGGAACGGAGAAC
 AAGAGGGTCTACATTAAATGCTGAAGGAAGGAAGGAAGGCCATTG
 TGTCACTGGCTGGCAATGTGCCCATCCACAGGAGCGGAACAATTGATCA
 ATGTGGAAGGAAAGGAAAGAGGTGAGGCTGTACTTCTGCCAGAAATCAGG
 CACCAAGACTTTCAAGGAACAGAGAGTAGCCATGGGAAGAAACTGGGA
 GAGGAGAGGCTGAGCTGGAAAGTGGCTCAAAGAGAGACACTCATTTG
 ATCTTCCTCAGTCACAGCAGTGTCAATTGGAGGCCCTGGATCACTCTT
 CTACCCGATTCCAAGAAAACAGGATTTCAGGCTGGCTGAGAGCAAAT
 AGCTTCCCCCTGAGTGTAGGCTGTCTCAAAGTCAGCAGCCTAGTTGCC
 CACACTCCTGTGCAGAGGCTTGGCTACTGTGGCACGATGCCAGGAGAT
 CACCAAGCTAATGATGGGTTACCGCACTGAAACATTGGCCCTTACA
 GCGGAGAGATAAAGTCTGCTGGCGTAAAATTCCCTACAAGGAAC
 CACCTGGCATTGGTGGGACGGATGTTGGGCAAGGGGGAAAGACTGGGG
 AGGGGGATGGACACATTATCGCTCCAGCAGTGTGTTCAAGCCTCAACAA
 CAGGAAGAGAGAACCCACAGGAGTTAGGCCATGTCCATCAAATGACCCC
 ATATTGTGGAAGAATTGACATTGCACTATGCCAACAGAGACTTGGGTGGAC
 ATGGTCTGGAGTGCTTGAGCCGTCAATTCTCAGGGTCACACTCTG
 TTAACAAATGCACTGGCCAGTGTCAATCAAATGTGCCATTCTAGGACCAA
 AGTTTGATATTCTTTAATATTGTTACTTGTGTTGATCATTG
 CCTTAATTAACTTCTACTTGTAAAACATGGAGAATTAGCAAGCTG
 CCAGGAGGCCAGGCAGGGAAACCAAGGATGTTCCATTACCTTGTGTC
 CATATCCTGTCCCTGGAGGTGGAGAGCTTCAGTCATATGGACAGACA
 TCACCAAGCTTTTGTGTGAGTCCGGAGCGTGCAGTCAGTGTGATCGT
 ACAGGTGCATCGTGCACATAAGCTCGTTATCCCAGTGTGCAAGAAGAT
 AGGTTGTGAAATGTGGAGCACATGTGTTAGGTATAAAATCAGAAGGGC
 AGGCCTGGTGGAGGTGGCAAATTGATTCTGGAGGACACCTGA
 SCATATACGGTCAAAGTGTGATGACAACACCACTAGGGATGAAGCTGGGA

GTGGGGTGGCTAAGAACCTGGACCTGACACTATTAGACATGGGTCTC
 CTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAGCTACTTAGGT
 AAAATGGTGAATGGTCATAACACTAGCCCACAGGGAGGTTACGAACCTCTG
 GTGACAATGTAAGTGAAAGGCCCTGAGAAAGAGTGAGGGAGTTGCAAAT
 GTCAGTAGCCATCAAGATCTTCTTTAAGAATAGTTCCACTAAAGAGATG
 ATTGCTTGGTTCCAGCCTCTTGTCTGGCTCCCCGCTGGGCCTTCT
 ACCTTAAAGGGCTTGGCTCTGGGAATTGAGTTGGCTGGGCTTGAT
 GACTTCAAGAGGACACAAGTGGAGATCTACTGCCTGCTCTGGCTAACT
 ACCTTCTCAAAAGATGAAGGGAAAGAAGGTGCTCAGGTCAATTCTCCTGGA
 AGGTCTGTGGCAGGGAAACCAGCATCTCCTCAGCTGTCCATGGCCACA
 ACAACTGACGGGCGCTGCCTGAAGCCCTGCTGTAGTGGTGGTCGGAGAT
 TCGTAGCTGGATGCCGCATCCAGAGGGCAGAGGTCCAGGTCTGGAGG
 AGCACTGCGGAGAGAGCGAGGGAGGGAGGCTGGTGAGGTGGTCTGCCAG
 GAACCATGCTTGACATCAGAGAGTAGAAAGCTCAGAGAGGGAGGAAAGGG
 CTTGAAAGAATCCCAGCTTCTAAAGATCATCCCTCTGGGCAGGCCT
 GGTGGCTCATGCCTGTAATCCCAGCACTTGGGAAGCCAGGTGGATGAA
 TCATTAGGTCAAGGACTTCAAAACCAGCCTGGCCAACATGGCGAAACCCC
 TTCTCTACTAAAAATACAAAATTAGCTGGGTGTGGTGGGCTGCACCTGT
 AATCCTAGCTATTCAAGGAGACTGAGGAAGGAGAATCGCTTGAACTCAGGA
 GGTGGAGGATGCACTGAAAGATTGTACCACTGCACTCCAGCCTGGGC
 AACAGAGTGAAGACTCTGTCTCATAAAACAAAACAAAACAAAACAA
 AATAAAATAAAATAAAATAAAAGATTATCCCTCTGAAGCTCAAGGAG
 GTTAAGGGTGTACTCAAGGGCACACAGCAGGTTAGAGGCAGACTCAAGAT
 TAGAATGTGGGCTTCTGACACCTTACAGGCTATTCTTTAGAATAATC
 CCATTCTACTTTGTTCATCTTTTGTCATGCCACCTACACCATAC
 ATGTATACTTCTCTATATCTTTGTATCCCTAATGCTGTACACTATG
 ATTTGCTTTCTATGCAGATGACCATACATTCCATTACCTATGCTC
 ACTCAGCAAGTATTCAATTCTACACTGTTCTTTCTTCTTCA
 TAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGTACTTTGTG
 AAATGTTACCACTTCCCTTATTCAAGAGAAGCTCCGTATTAAGGCTTCA
 CTGAGGGTGCCTTAAGGCATGATAATGGTCAAAGGCTGAAAGACAGTT
 AAAGAGACCTGTAAGTCACAAAAGAAAGTTGAGCAGGAGAGAATTCCT
 GCCTGGAGCAGGCCAAGCTGCTGGAGAGGCAATGGGGCAAAGGCCAG
 GCAGACAAGCCAATGGGCTCTCCACAGCTGCAGCCAACAAGTTATGCC
 AGTCTAAAACCTCTAAAGAAATATGTTTAAACAAGATTGAGGACTGGA
 TTATGAGGCTAGGGGAGGCTATCACAAACTGGAATAAAATAAGCCAGAG
 AAAAGTGGCTGCCCTCCAACCTGCAACTGACCTAGCTAGGCTGATGGC
 TGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAGAAGGGACAGC
 AGGAATATAACATGGCTTTGTAAGGATGAGTCTGAAAAATGACCATT
 GCTGCCAAATGCCCTAGCTACAACGAAACTATTCAAGACTGGAGGT
 TGCAAGGATGCTGGAATCTCAGAGATCATCCAGCTAGGCCCTTATTTTC
 AGATGAGGTCCAAGGGGAAATGACTTGTCAAGGTCAAACAGCAAGT
 GAATGGTTCTTCAAGTCTCAATTCTATTTGTTATATCATCTAT
 GTCTTGTGTTATAAGCTCACCCAGGTAGCAAAAACATATTCTACTCA
 AAAGGGTAGACATATGTTAGTCTCAAGATCATCTTGGTTAGAGT
 TTAACTCAAGTGAATGGCATAGGCTGAATCCATCTTAAAGGATAATC
 AAATTATGTTGAAGACTGGTTGTCTTCTACTATGAAATGGAAACAT
 TATCACTACTCCCTCCCTGTCAACCACCAAGTGTGGCCACCACCAACG
 TTAGTGAAGTGAATGTGGTGTATGATGACCAAGTGGCCAGGTCAAGT
 GGTGCAGCCTGTGTCACTGGAGAGGTTAAAGTCTTCTAAACAGGTT
 TACCATGGCATCAAAGTGGCCAGAACTCCCTCTTGTAGCTTCCCTGT
 GTTAGAGCCCTCTGGGTGGAGTTAAACCCATAGTCTTACCTCAT
 CTGTTAGGCCATCAGCTCAAAGAACAGTCATCTCATGCCACTGT
 AATAAAAACAGGGACATGTCTCAATTATGTTCTAAACAGGTT
 TCTCTCCCTGTGTACAAGACTTGTACTGTTCTAAGAAACTGCAAACAGCC
 TGCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTACAGTGATATGCG
 CAGAACAGTCAGAAGGCAGATTCTAGGCTGGCAGGTGGCACCCTGG
 TGCTCCCTGTGGATCTTGAGGCCCTAACCTCTAGCCAGCAGAGTCAGCT
 AAAATCTGAGCTCTCCCTCTCCCTCAAGCCACACTTGTCAAAGGGATT
 CTTGTATTGGCTTGGAAATCTTTCTCCCCATTGCTCTGCAGGAAG

FIG. 3 (43 of 52)

45/118

CCCTTGCAACAACACA TGGATAGCCTCCAGGTCCAAGGCTGGAGG
 CTTGTAATGGGAAAGTAGTCTTAAATCAGATTACTGGCACCGTGT
 GCCACTGAAAGAGGCCATTAGGGAAAAATCTGGCTCCAAGCACAGAT
 AACACTCTACTCTTGAAAGAGGAGACCTGCTCATGTTACTGGCTCAGCG
 TCTCCACTGACCTGTAATAAGCCATCATTCACTGGCGAGCTCAGGTACT
 TCTGCCATGGCTGCTCAGACACCTGTTAAAAGGAGAAAATGAGTGAC
 TTCCCCATGACGGCTACGTTCATGTTGATTTCTCAGCATCAGTGCA
 TGGCAGTCATGCAAAGAAATGATCTGAGTAAATGAATGAATGTGTGAA
 AGAGAAGTCCTTGGGTCTAGAGAAAAGCATTTGCTAAACAAACCCAA
 CTAGCAATGTTAGGCTAGGAGAGCTGGAGCAGAGGCTTGACACTAAC
 TTTAGGGTGTAGCTGTTAGATAAGCAGTATCCATTCCCAGAATATTCC
 CGAGTCATAAGCATTATATTACACCTGGCATTGGCAAAAAGCTGAGAG
 AGGGAGGCAGAGAGGGAGGGAGAGAGACAGAGAAAAGAGAGAGAG
 AGAGAGAGAATATGCATACACACAAAGAGGCCAGAGACAGAGAGACTCC
 CTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGAGCAATGAAGA
 TTGGCTGAAGAGAATCCCAGAGCAGCTGTTGTCCTGTCCTCGAAGA
 GGTTGGTATCTGCCAGTTCTCCCTGCTGTTTATAGCTTCAAAAG
 CAGAAGTAGGGAGGCTGAGAAAATTCTCTGTTGAATAACCTGATTTCACAAT
 CAAGTTAAAGGAAAGGGAAAAGAGTATTGGTGGAAAGCTTCTTAGGGAG
 GGGACTAATAAACTGAGATAATTCTCTGGTCATGGAAGGGCAAGGAGTA
 GCAAACATGACACATTGCAAATGTATCACCAGTCAAATATGCAATTG
 TTCTGACAAATCGTTGTCAGTTGATGTCACATTAAAATACTGGATT
 TCCACGTTAGAAGAATGTTAAATTAGTATATGTTGGACAAAGTGGAA
 GACACACAGATTATACATGCACACATACTTTCTTCATTCACTTCTTGTA
 CTTAAGTTAGGAATCTCCACCTACAGATGGATAATGGTACAATGA
 AGGGCCAAATAGCCCTCCCTGTCGTATTGAGGGTGTGGGTCTCACCTG
 GGTGCTGTTCTCGCCTCGGGAGCTCTGTCATAATTGCAAGGAGCCTCTGA
 GGAGAAAATTGACCTTCTGGCTGGGAGAGAACATACGGTATGCAGG
 GTTCAGGCTCTGACGGAGTTGGGCAACCCCTGGAGATAAGCTCACACAA
 CCCTGCAAGACCAGGTGCTGTTACCCCTAGCCAATCTCATGGATGAACCA
 ATCAATGCCAGATGAGCTCTGCCAAAATGATTGGTGAACCTCTGAA
 AAGTGGAAATTGTTCTGTAAGAATATCCATCTGAGACTCTATCTTGTG
 GTAATACCAAGAGTTACAGTTCTCTTTAACCGAGACACCAGCAAAGTG
 CCTGCTCAGGGTAATGCCAGGGAGCCCTCATTGAGTGAATGA
 GAGTCCAGGTTATGAAACAGTGCCTGGAGTGTAGGAACACCCCTCTTG
 TCTTGACAGGCTGTCATCATAACACTTTTTTTTTGAGACAGAG
 TCTCACTCTGCGCCAGGCTGGAGTGCAGTGGCAGATCTGGCCCC
 GCAAGTTCCGCTCCGGGTACACCATTCTCTGCCAGCCTCC
 GCAGCTGGACTACAGGCACCTGCCAGGCCAGGGCTAATTGGTAT
 TTTAGTAGAGACAGGGTTTACCATGTTAGCCAGGATGGTCTGATCTC
 CTGACCTTGTGATCTGCCGCCTGGCTCCAAAGTGTGGATTACAG
 GCGTAGGCCACCGTGTCCAGCCTGTAACACTCTTATAGCACTGAGTTGA
 AACCTTGCTCCTGTTCCAGGAAACTGAAATCTTTGAGCCAA
 GTCTAGCACAGTGCCTGGCATGTCATTCAAGGTTAGAGTTGCTGCTT
 GAATGGGTGAATGGAAATTGACAGCATTGAAATTAGTATGTG
 CAGTATCGTGTGCTGTCATTCAAGGAGTGTGAACTGCTCTGCAA
 GTATTGAGACAGGAGGGAAATAGGTTCTACTGTGGGAAAAAGAGCATT
 CATGGACTTGCTCTCAAGCAGCCTCTGATTTAAATTGGCTCCAGT
 ATCTTGATATCAGGAGTCAGTCACAAGAACCTCATCTTAGTAAAGTTA
 TTTCCACAGGAAATCTAAAGCTGTTAACATGTTAGTTCTGTGAAT
 TTGATAAGCCATAATCATTCTAACACTGAGCCCTCTGAAATTGGTG
 TCTGGTCTGTCAGATAGCTAAAGCCCTGCTGGGCTGGCCTAGGGACTCC
 TCTGTTTGCTCCACAGGATCCACTTGCAAATTAAACACTGGTCTCC
 CGTGTAGGAACGTGCCACCTCCTCAGAGCCTGTCTTCTTCTTCTT
 CTTCTTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
 TCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
 CTCCCTCCCTCCCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
 CTTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
 CTCCCTCTCTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT

FIG. 3 (44 of 52)

46/118

TCTACCTTATCCCC...GCTGGAGTCAGGGTACAATCATGCATTCA
 TGCAATGATCACAGCAGCCTAAACCCCTCCTCAGAGTCTTATGGGGCAA
 CCAGCAGGGCTGGAGGGTTGGCTCTGTGAACTCTCCTGACAGAAC
 CAGAGATGTCTTGGTCTGTGATTACAAGCTGAACGAAGGAAGA
 TCAAAGCCAGTGACAGGAAGGGAGATATGCAAGGGACCCGAGCAGCT
 CTGAGTTAGTCCATTCTGCTTCTGGACTTGGATAACAGGTAGAAACCT
 TGAGCTTCTACTTCTCCATCTTCAATTGAGCATCCAGGACCTCAGAAT
 CTGCCAGCTAAGAGGAGCCCTAATGATTGCTGGTGGGATATGGTGGGAC
 CACAGAGATGAAGACATGAATAGCTATTGAAATGTGAACAGCAGACGAAG
 AAATCAAGGCAGGGTGGAAAGTGAECTCATCCAATAGCACAGTGTGGT
 TGAAGCAGCACTAGTATCCAGGTGCAATGAGCCCCTGATGCTTCGCTCG
 AGGGAAATTGGAGCCATGGGCAATGCCCTGACGTAACAGTCTCCA
 CAGTTCTGCCATGTCTCATCCTGCCCTGTAACCTGGACCCAAATCTGCT
 ACCATCCCCTCCATCTCAGGAAGTGAAACCTTATGTCAAATAGGTGT
 GCAACGTATGTATCAGATCCTGCTTCCAAAGGAGACCGCTCAGGCCACA
 GCACTTCCCTCCGATCCCCAATGAGCAGAAAATATCTGCTATAAACATA
 GTTGGCACTAAGGGAGGGAGTGGAAAGAGTGTGATGATGTAGATGGTGT
 GTAGCCCCAAGGAAGTGGAAAGCAGAGATGGGAGCTGGAAATGCCAG
 GATGCTCCAGCTTTGGGAATTATTGAGCTTGTGAGTCATAAAGCCTT
 TCTCAGCTGCAAGTCTCTTACCCCTGTCAGGTATTCTCCAAGACAG
 GAGACTGACATTATTCAAAGCAGCAAGTGCCCTGATACCACCTTGTGTC
 TAATCATGGGCTTCGCAGCCAGTTCAAGGTTGATCTCATCTCATTGGT
 CTTCATTCATTGAACAAGAACAGCAAATATCATGGGTTAGTT
 TTATATTATTGTGTGACATGCAGTGATGTTCTGTAGTGGCTTGTGAGCTG
 TTCCTCCCTGTTCACCTCTGCTTAGAACAGAACTAACATCTGCC
 CCAACATTTCCCCAATTCCCATCTCATTCTGGCACTGGCTTCTAAT
 ATTGTTCTTATGAGTCATTCTTGTATCATTCCATGAGTCCCTCTGG
 GATCTTAAAGTATGAAAAATGTTGTGTGACCCACACCTGCTTGTGGA
 TATTCTCTCCTTCCCTGCTTCTGGATTATTGGAAATGGGACT
 ATGATTTTATCATATCGCTTCACTCCTTATGGCATCATCTCAATG
 GGCTTCTTCTCCCTTGGATCCATCAGAAAAGCCCTGGGGTAAGATGG
 ATGGCAGGGCTCTCCTACTCTATGTCTTCTCACACCTAGTGGGTATAA
 GAGAGGGGACCACAAACAGAGGGGCTCTGGTACCAATTCCAGGGTCT
 GGAAACATTTCTGAAAGGGCAGATAATAATGTTCAAGGTACAAC
 CTCAACCTTGCACTTCAAGAAAAGCAGTCAGATAATAACATAAAATGAAT
 GGGTGGCTGGACTTGTCTGGTCCCTGCTTATATCATTGTATTA
 TATCATTCTTCTTACATACAAATTAGAACAAACTTAA
 GCCGCTTATTGAGCACCTACTAAGTGCCAGGTACCTTTTCCCT
 ATTATCTTATTAACTCTCATAATAACCTTAAAGTAGATAATAATTGAAC
 CATTTGACCTATGCAGAAACTGAGGTGAGACAATAATTATTAAGACC
 GCACAAACAGTAAATGCTGGAACTACGACTCAAATATGGGTTACTGAAC
 CAAAACAGATCTTATTCTCACTTTAATTGTTACATATGTTATTGC
 CTCATCTCTGTCCACATGGTGCCATCGGCAGACTCCTTCTCATTCTC
 AGTGATTGAGTGACATTCTAAACTACATTGGCTGGCAGATTCACCTCTG
 TCCCTAAATGTTCCACATTGCTTCTTAGGATTGAGATCCTCTGTT
 CCCCTGCTTCCCTCTTCTCTGGCGGTGACGTGCTGTGAAATT
 TGTTCTTCTCTCTCAGGGTAGTACTGGGACTTCCAAATCAGGGTT
 TTAGTGATCTCTTCCCTTCTGAGTTCTCTTATTCCCAATTCACT
 TTCTCATCTATAAGTGGCAGCTTGTGCTGGAGGATTCTTGTGCTT
 TTATTCTCTTAAAGACTTGTGATAACTGTCAAAGCAATCCCTGAAAG
 GTATCTGCTTGGAAATTGTGCTTATGATGCTGAAAGAAACTCTCTTC
 CTAAGCTATTATAATGCT

>Contig42

GGCTAGCTGCAACTCTGAAATACAACACATTGAGACATGCACACACTTT
 CTGGCTCCAAAAAGAAAAAAATCAATTATAATAATTCTGATCCT
 TTGCTTATTCCACAAACTCCATGAAAATTGTACATTGTCCAAGCAACAT

TTCTTAATATTCTTTTCTCTGCTGTC
 CACCTATCTCTTCCAAACTCCCTGTAAAATCCCTGCCAGCGAACCTT
 TATTCAATTGGAGGGCTGCACTGATTAAATTAAAAAA
 AAAAAATCCCTACTCCATGCCCAGATCCCTAGTTGTTTTGTTTG
 TTTCTGAGACAGGGCTTGTCTTCCATGCTGGAGTGCAGTGGCATG
 ATCATGGCTACTGCAGCCTAACCTCTGGCTCAAGTAATTCTCTTGC
 CTCAGCCTCCCCAGTAGCTGGGAGTTCAAGGTATGTGCTACCATGCCTAGC
 TAATTCTTCTTTTGTAGAGACACGGCTTGCCAGGTTGCCAG
 GCTGGCTAGAACCCCTGGCGGACGTGATCCGCCTGCCTCGGCCTCCCA
 AAGTGGTACAGGGATTACAGGCGTAGGCCACTGCTCCGCCCTGGGTGCAA
 TTTGAGCTTCTCACTTATTAGTGTAAAGACATACAGCTAATTCTAAATC
 TTCCAAACCTCAGATTTCATCAGTGAAGTGGAGGATTATTAGAGCTC
 ACTAATAACATGGCTCAAAATATAATGCAAATTGAGATCAAAT
 AATAAAATCTATATTACATGGGAGATCTTAATGTACCTTATATTGA
 TAGACTAAGATGATCAAAAAATAGAAAGAGAGCAGTAAGGAGAGCAAGC
 ATTTAATCAATAGGACCAATACATTAAATCAATAGGATCCTCAGGAATA
 TATACAGAATACCAAACCTAACAACTGCAGAAAACATGCCAAACATTAG
 GTACAGACATTGGAAAATGCAATCTGAAACGAGTGGACTGACATT
 AGAAGATATTAATAAGAGCACTAATGATGGGATTGCAACCAGTCTT
 CTGACTTCCAGAAGCTTCTACAGTAAACATGAAATCACATAATTCTC
 CACTTCTACTGTTCTGTTCTGGGCTCTGCTCTGCTACTGTCTAAT
 ATCTTGGCCCTTAAAGTTGCTAATCTTCAAACCTCATTCTGTGACT
 GGGCGCTGGCCTTGTCTGGGCTTGTAAACTGACTGTACACTTA
 TCTGGAGCATCCAGTGCCTACCACTGACCCAGATTCTCATTGCGCTCC
 TCCCTCTCCACCTATTGAAATTGCTCATACCGTGTGAGACCCCTCCC
 TTTCCCCCATCTGAATTCTTATCAAGACAACGCACTGCCATACTCCCTC
 GTACCCCTGCTCTGGCCTCAGACTGAATGTTGTTCCATTGAGGATCTG
 CAGCTGCATCAGTTCCCCAGCACCCTGAGCATGGCTAGT
 CCTAAAGCAGAGAATTAGCCTTCTATCCCTGCTGCTATACATGCTGGGA
 CAAATAATAAGAAATGACAGCATTATGATAATGCAAGGCTGAGGAGGC
 AGGAGGAGGAATCAAATTGCTTATCAAATAGTGTCAATTCTT
 AATATTGGACTATAGAATATGTCATGGATCTATGCTCAGGTGGGTTCCCT
 ATTACTCACTCCACTGAGGCCAGGTTGTTGAGGATTAGCTGTCCAAGAGGG
 GTTCACTGCTCACAGCATAGGGCATTCTGAGAATTACTGGCCACACTT
 GTGTGGAGACCTCCAGAGAACAGAATCTGGGTTGGCCTGACTTCCA
 GGAGGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAGAGGGGAAGGG
 CAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGCCAATCAGGG
 CTTCTAGCTTTGGGCAAGGAAACAATGTTGGGAAGCAAAAAGGACAA
 TTTCTCTCCCTTGCATGAAGACTGAGCAGTTTACCAAGATTCCAGG
 GAAACACCCTCCACTCTGGGTTGAATGTTGAGTGAAGAGACATTCAAGCTGG
 AACACTAGAAAAACTATTCTGAGCCACTCACCTTAGCCCTAGAAAGT
 GTTGGATTGTCCTTCATCTTGCACAGTAGAGACTGCTGATAGCATCA
 GAACCTGGGCTCTGGAAATTAGACAGATATGGGTACAAATCTGAGCTCT
 CACTTATTAGTGTGGGATGTAGAGCAACTTTAAATCTTCAAACCTC
 AGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCACCTAATAGGG
 GTTTTGAGAATTAAAAAGTTATTCAATGAACAGCATTAGCAAGATGC
 CTGACCATTTGAGAAAATAACAAATTGTTATTATTATTGTTATTAAA
 CATCTTCTGACCTCTGACTGGGGCATCGTATCATCAGAAATACTT
 AGGATGGGATGGATTCTGCATGGCTGAGTCAAGGGTGAATAATGGAG
 GAGTGAAGAAGGAAGAAATGGAGGCCAGAAATCCCCAGGAGCCAGCATGG
 TACAAGGCTGAGCTAGTGTGCAAGGCCTCTGGAAACGCCACAGAGCT
 TGCACTGGCCCTGGGAGGAACCTCTAGCTGGCAGGACCAGCCACAA
 CAGTGGCCAGGGGATTCTCCAGGGCTGGCTCTAGGAGTTCTTGG
 CCAAGCCTGCCCTGGAGAGGGTTATAACAGGGATCTTCCACTGGCAG
 GTGATTTCACCCCTCGGTGAGAAGCTCAGGCATTGTTGATGGAAGGTGG
 AAGGCCCTGTGCTGGGCCAGTGACTATCAGGGATGGCGGGTGGCTGGAA
 AATAGCAAATAAGACAAATATGATAACACAGTTAACCAACACTATGTGA
 AGCTACAATATGGGTATCTGTAATAGACAATTCAAATGTAGAGAATAATT
 CTAAGGTGTATTCTCCCGCCAATGCCATAAGCACACGCCCTGCCTG
 GGTTCTACTGTGGAATGTCCTGGTCTCTCATGCCAGAGGTGG

FIG. 3 (46 of 52)

48/118

GAAGTACTCCTACTTT.. .CACCGGCTTCCTGTCACTCCCTGCAGC
 CCTCAGCCCCCTCTGCACAGGGAGGTTCTCCCTGCTGCTGCAGTGCTT
 TGTACTTGTAGGGTACCTGCACACAGGTATTGGTGTCTTGCTCAC
 ACCCTACATCACTGTAAGCTCCCAGGAGCAGGCTCTGTTGACTCAC
 CTGTGATCCTCCACCTCCACCTGTAGTGCCTCAAGCATTGAGGACAAT
 CACTGGCTGCCCTTAACCCAGAAATGCTGCCAGACAGGAGGCCATGGC
 CCAAGTCTGGAATGGGTATTACTATGTCAGCACAAAGGCCCTTGAC
 AATGAAGGCTTAAAAATGCAGTCCTAGTCAGGTGGAGGAGGGCTTATA
 GGATTCCCAGGAATCTGGATCATCTCTTGAGAGCTTCCCTGTCTCG
 TTAAAATCACATCCTACGGCCAAATAACAAACAAAAATGGATGTAAT
 TCTTGAATAACTTGTGGATGGGGACAAGGCCACCCCCAGATCTGC
 CAGAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAGTCTGGTATCAGAGA
 GGATGCCAGTGACCTGGGACACATGCCCTTGCTGTCACTCAAGGA
 GCAGCAGCCTGGCCCCGACAGTGACCAGGACCTGGCTCCACGCTG
 GGCAGGAGCTGGTGTGATGAAGGGAATGCCCTGGCAGCACGTGCT
 GTCTCCTCGTGTGAGCTTACCTGGCTTGCTGCGAAGAGGCCACTCGC
 ATTTCTCAATTTTTATTTTAAATTTTTAAATTTTTATTTTATTTT
 TATTTTATTTATTTATTTAATTTTTAATTTTTAAATTTTAAATTA
 TGCTTTAAGTTTAGGGTACATGTGCACATTGTGCAGGTTAGTTACATAC
 GCATACATGCCATGCTGGTGCCTGCACCCACTAACCTGTCATCTAGC
 ATTAGGTATATCTCCAGTGGTATCCCTCCCCCTCCCCCACCA
 CAGTCCCCAGAATGTGATGTTCCCTTCCTGTGTCATGTGATCTCATTG
 AATTTCTTAAAGGTGGAATCTCTAGTGGGCTAATCTGTTAGAAAT
 ATCAAAAGAGATCCTGGGAATGACTGGATTCCAGAGTCATCTGGTAA
 TCCTCATAAAACAACACTCTGGATGTCAGCACATCTCCACCTTGAA
 CGCAGGAGGCTGGTCAAATGGAGGAGCAGCCTACTGCACCTTTTT
 TTTTTGGCCTAAAGTGCAAAAGGGGATACGTTCATGTAATAAATCA
 ACTGCAAATCGCTAGTTATGCTGAGCCCTGCGTGTGGACACAAA
 GGAACCAAAGGTTTCTCCCCGCCAACACACACATAACACACACAA
 AATCATAAAACATACATACCCCCAACACATAACAAACACACACAC
 ACAAAATATACACACACACACACACACATGCCACAAACCTGTGTC
 CAGAGATAGCTACTGGGGTTGTGGCTCGCTGACTCAAGAATG
 AAGCGTGGACCTCGCAGTGAGTGTACAGCTTAAAGATGGCATGGA
 TCCAAAGAGTGAGCAGTAGCAACGTTACTGTGAAGAGCAAAGGACAAA
 GCTCCACAACCCAGAAGGGACCCAGCAGGGTGTGGTGGGGTGGC
 CAGCTTTACTCTTTGGCCCTCCATGTTCTGTTCCATCCTATCA
 GAGTGCCCTTTCAATCCTCCCTGTGATTGGCTACTTTAGAATCTG
 CTGATTGGTCATTTACAGAGTGTGATTGGCGTTTACAATCCCC
 TGTAAAGACAGAAAAGTCTGTGATTGGTGTGTTACAATCCTTGTAA
 ACAGAAAAGTCCCAAGTCCCCACTGGACCCAGGAAGTCCACGTGGC
 CACCTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAACAT
 ACATACACAAAGTATACATGCATCTCCCAAATATACACATACACAGAA
 ACATACACACAGGAACCTAGCTACCTGTCAAAAGTCTGCATGGTATTG
 CTCTGCAGTGAGTAGTTAGAAAAGTGAATTGTTCAATAAATTGGAG
 TCCTTAAAATCGTTGTAAAGATAGAAAATTTAAAGTATATAAAATAA
 AATATGTATGCTCTTGGCTAGCATTACACATGTAGGAATTATCCTA
 GTGGAGTAATCAATGATATGCAAAGATTTGGACAAGCATATTAAGC
 AGAATTATGTATGCATATGTGTGTATATATATATATCTCATA
 TAATAATGTAAAAGTGAAAATAACTCAGATGTTCAAAATTGAGGATTAGT
 TAGACTATGATCTGTCATATGTGACATACAAGTTAGCTGCCCTTATT
 TCTCGAGCTCAACCTCTATAAACAGTGTCCCTGTATATCAGTATTG
 TACAGATAATCGAACTTATTGAGGTTTACATGGGCAATAAAGGCAAGA
 GTTATGAATACTCCATACTACACTAGGTAGCACCCCCCTATTAAAGACAA
 ACTCTCTCTCATTCCCTTCCGGAACCACTGGTGAATCTC
 TACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCGTCACTC
 ATCTCCCTGCTGAGAGCAATGGCCTGCTGCCCAACTCACATCCT
 CATTCAATTCCAGAAGTGGAGCACACAGAAGTGCCTACAGTACCCCAACC
 ACCCTCTTAAAGATAAGTTAGTGTGTTGACTTTAAATTTTA
 CTTCCCTTTCTTCAACATCTCATCCCACAGAGGTTATCAAGA
 AGTTCTCTAAAGATATGTGTCTCTTATGGAATTAAAGAAATCAGGGA

FIG. 3 (47 of 52)

49/118

ATGAAATCTAGULATT AGGGATAACATTTCAGGTCTTAGAC.
 ATAATGGAATACCTTGCACTAATTAGATACACTATTGTAGAAAAGTATTG
 ATGAAATGGAACGATGTTGAGATATCATATTGAGTAGAAAAGGCAAGAT
 ACATTAAGTAGGAAATGTATCTTACAAAATAATTGTCAAGACACACTCCT
 ATATTGTATGTTATATAATCGCTATGTGAAGAAAGCTAGAGGATGAG
 ACCACAGTCTTGGTGAAGTTAACAGATGATGCTGCAGCATGCTCAGAA
 AGGCTTGGTATAGTTTCCAGTAATTAAAGGACTGATCTTAGGTAATT
 GPCCATCCTCTCTAAACTGCACCACCTTTGTCGTAAAACAGGAAGGGAT
 GGTATTTACCCCCAGGGTCACTCAAAGGATTGGTGGAGAAAAATAATA
 AATGGGCTGAGCCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTATT
 GTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTCCA
 GAAGCTATTACCTTAATTGGTATGTGGATTCCCTCATACTGAGCAGC
 TGTGTGTGGTGTGAAAACATAGCCATACACAGTAACTGACAAGGGCAA
 ATGTGATGAAAAATGCAAGGAAGTGCAGATAATAGCTAATGGGCTGTA
 GAAGGAAGCTAGTCCTGGAGGGCTTGATCAAGGAAGGTCTTTGCATG
 TCACCTTGAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCGGAGT
 GTACCTGGAAGGGAACATGAAAAGAGGACATTTCCTGGGACATGGGG
 ACTCCACTTGCATGAACTCTGGAATTGGGCAAAGAACCATCATGAGAAC
 AAGGGCTTCTGAAACCTCCAGGCTCATTGGCTGATCTAAACCTGTGT
 CCCCTTTCTTCACTCTCTGTGTTCTATACCTGTATTATGGACT
 GGACTGGAAGGCCACCTGATCTATCACAGTACCTGAAATGTGTTGATA
 GGTGTGGCACAGTCCTAGCAGAGTGGCACTACCCCCACAGGAATTGTT
 TATACCTTGGCATGGAAAATAGCAGGAATGAGTGTGACTGATAACTG
 AGGATGCTATTATTATTGGCAAAGGAATACTTGTGTTGATTGCTATA
 ACCACTCACAAACTGTGATTACAAATGAGTACCAAGACCTAGCTCTTCA
 AGTAAAGGATCTTGAGAACTGAAGGAAACAGAGCTCAGGAGTCCAAGA
 CAGAGCCACAGACCACGAGGATCCCTGGCCAGGTAGGTGGTCTCCTGC
 ACTGGCTTCAAGGCCAACAGGATGGATGGGAAGTAGAGTAGCATCTGG
 CCATCTAGACCCCTGCTTTATCCCACTTGGAACACATCTGAATTCT
 AAATATGATCTCTGAGACCTGCCAGAACACCTTGCTCTCAGCCCCAGTA
 GCAGCCTGCTCTCTCCAGGAGGGCTTCACTAACAGTAGGGCATTGCT
 GGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCTGGAAATGC
 TAGTCCCTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAATA
 TTGGCCTGGAAACAGATTGAGTGCAAAGAGATGGACTTCAGATGGC
 CAGATGCACTGCTTCTTGTGAAAGCTCCCTGCATTATC
 TTAATACAGGAGCAGATTCTGAGTACCCCCGAGGGATGGCCCCAGGT
 CCTCAGCCTGTGAGCATTCTGCTCCTCAGCAGCACCAAGTATCTT
 TATATGTCTTGGACACTACGTTCTGCCAGACATCTCTGCTCTGATG
 TTCTGGCTGCAAATTCTGTCAGCGCCTCAATTGGTGTGCTCTT
 GATTACCCAAACATGACAAGGAGTGTGCTCATGATTCAAGGATA
 CTGCCAACACACAAACAGGTTAAATCAAATAGCAGATACTTGTGCT
 AAAGACCCATCAGCTAACCCACCTGCTCCTGCTCACCGTCTTATTGTT
 GAGTCCTGAAGCCCTTCTTGTCAAGCGCCTCAATTGGTGTGCTCTT
 GTTCCCTTGTCTACTCTAAACCTTCTCAAAGGATTGGATTGTACA
 CAAACTGCCATCTCTGCAATTGAGTGTGATGATTCTGAACAAATC
 ACTTAACCTTGATTTTATTGGTAAGATGGAAATACCAATTGGCTC
 CACTCTGCTCTATGTTGGCTGGCTGATGTTGAAAGCTCTGGTCAAC
 TGAGATAGGGTGTGCAAGATTATATATAAAATATATCTCTCCAACCC
 CTCCAATGAAGCAAGTCACGTGAGTCATTCTACCTAACAGATATTAGGG
 ATTGAGCCTCTGGGACATTGGTGGCTTAGGTTTCTGAAAAGAGGTT
 GCAGAGCACTGCTTTGTGAGGCAAAGATTAGGCTACTGCAGAGACTC
 AGCAAACCTCTATAGAAGGTGTCAAGTGGTAAGTATTAGGCTTGTCTT
 GCCAGATGATCTCAACTAGTTAACCATGCTATTGTAGCCTCGAACAG
 CCAGAGACGATCTGAAACAAGAGCATGTTAGTGTGGCATAAATATAGTA
 CCGCG
 >Contig43
 GCAATAAGTCTATTTACTGTAAAGTTAATCAAATTACATTCAAGAACAC
 TTAATCTGCAAGAGTCCTTCAAGACCCATACCTAATTGTGTTAC
 AATTATATTTGTTCTTAAAGAAGACCAATATAAACTATATCCA
 GCCTCATGATAAGTACATAAGAAACTATGCAAATAAGGGAAAAAAA

FIG. 3 (48 of 52)

50/118

CAAAGAAAATACCTA...TACTAATGGTCACTTCTGAATAGGACAT...
 TCATAATGATAACAAGCACTCATTACTAGTCTAGGAAATGAAGATATAAT
 TGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGTGGTATAGAC
 TAGGGCAGGACAAAGAACCTAAACCTCATTCTAAAGATAATTGTTAA
 TACGTAAAACCTCAAACAGTAACAGTAAAGCGGTCTTAAAGAA
 ACAAGCACTAAACACCAGATAGGAAGCAGAGATGGGGAGAGGGCAAG
 AATCTGATTATTTTGCAACAAATTGTAAAACCTTGTACTGTTAC
 ATGTAGAACTTGGATCTTTTAAAAACACAAAATAATAACTATTAT
 TTTTAACTGGATTTGAAAAGAAGATAAAAGTCTCATTTAGTAATT
 AAAACTCATTCCAGGTAGTCCACTCAAACCTATATTCGAAAATTAAAA
 CTTTGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGAGGTTGAGACC
 AGCCTGACCAACACGGAGAAACCCGTCTACTAAAATACAAAATTAG
 CTGGCGTTGTGCATGCCTGTAATCCCAGCTACTCGGGAGGCTGAGGCAG
 GAGAATTGCTTGAACCCGGAGGCAGAGGTTGCAGTGAGCCGAGATCACA
 CCATTGCACTCCAGCCTGGCAACAAGAGTCAAACCTCCTCAAAAAAA
 AAAAAAAAAAAATTAAAACCTCTGAAAGTTGAGTTGAGATATTGAT
 TATGCTCATTTAACTTGTATGTTGAAAATGTATGAGAATTGAA
 GGTTGGGGATGAGAAAAAACATCAACCCACAGCCCATTCAA
 TTTTCAGCCCACCCACAGCTCCGGGAAGGGCAGCAGGTCCATCCTTCA
 CTCTTCTTCACCTCTTCCCCCTCTGCTCTTCACCTCTAAGTTG
 GAGCCCAAGAAGAGGCACTGGGAAATGGAAAGTCTTGTACGGTAC
 TTGCCGGGAAGCTGCCATGAAGACCTGGCCCCACGGTGGGAGGGAAATG
 CCCAGCTGAGGCCTCGTGGCCATGCTAGGATAGACTCGTCCAGACATGTC
 AGGTGGTCTGACAGGGCAAGCAGCAGGAAGTCACTGAGTATGAACTG
 ATCTGTATGCAAGGGCGGGAGAACACGCGGAGGAATGGGGCTGAGAAA
 ACAGCACAGTACGTTCTTAGCAGCTGCTCTGCTCAGCCATGGGAGTC
 ACCAGAGAAAGAGGCTGGAGGGCTTATTTCACTGAGTACCAAGGGAGATGCCCTCTTCC
 ACCCCAATGCAAGATGGCACAGGCCCTTAAACACACACATGGTCTCTCA
 GAGGAGAGAGGCCCTCACAGTGGACACCCGATTCTCCCTGGTCAAGCAG
 CAGCAGGGCGAGTGCCTGGGCATCATGAAGCTTCACAGGAATGAGCTCT
 CAGCAATAACAGGAACAGTGCCTGGGGACTGTAGCTGCAAGACCGATT
 TCATGTAAGATGGCTCTGAGGACTCCGAGATAACACCAGGCTGAGACTAG
 CTGGCAGCTCCAAGTCTTGGTCAGAAGAGAACAGGAACAGGAAATTG
 GAATTACTGTTACTACAATTCTTACATCCGCACAACCATGAGGTCCAG
 AGAGTCTCTTATTTTTAAAGACAGGGCTCACTCTGAGGCTTACAGTCT
 GCCTAGAGTGCACGGTGTGATCATGGTCAGTACAGTCTCACCTCC
 GGCTCAAGTGCACCCCTGGCTCAGCCTCTCAAGTGGCTGGACAGCAGT
 TGATGCTACAGGCCCTGGCTTTTTTTTTTTTTTTTTTTTTTT
 TCGGTAGAGACTGGCTCTCTGTATTGCCAGGCTAGTCTCGAACCT
 GGGCTCAAGTGCACCTCTGGCTCAGCCTCCAAAGTGGTAAATTACAG
 GCATGAGACACTGCACCCAGCAGTATAGTCTTAAAGCTTATTGAG
 GTACGGCTAACATTGAAAAACTACACAAATGTAAAGTATGCAATTGAT
 AATTGACAAATGTACACACCAGTGAACACTACACTACAGTCAAATAA
 TGAAACATATCCATCACTCCAAATTCTCACGCCCTGGTAAACCCCT
 CTCCCAACTCCCTGCCCTAAACATCAGACAACTACTGATGCATTCTGTC
 TCCATAGGCTCATTTACATTCTAGAATTTCACATAAAATAATGACAG
 AGTATATACTCCTCATGTTAGGCTCTTCAGCCAAATTATGCAAGAT
 TCATGCTTATGGCTGTGCGTATCCTAGCCATCTCTTGTCTGCTGAG
 TAGGATACCATGCAAGACAGACCACAGCTGCTCATCCATTCACTCTT
 GACAACGTTGAATTGTCTGTGTTTGCAATGACAAATAAGGGTGTAT
 GTACATTCTGTATAGACATTGAAAAGCACAGCATTCTTGTGCTGAG
 GGTAAAGACCTAAAAGTGGAAAGGCTGAGTCATATGGTAAATATATGT
 CTAACTTTAAAGAAACTGTCAAACGTGTTACCCAAAGGGATTGTACAATT
 TTACATCCCCACCAAGCAGTGTATGAAAATTCCGTACTTCCACATCCTCA
 CCAATATATGGTGTGGTCAATCTTTAAATTGGACATGNTAATGAGTG
 CAAAATGAGGCCAGAGTGTCAAGTTACATTGTATCCTTTGGCAT
 CAAAACAGGGTGTCAAGCATGAAAAACACTGTTCTTGAATGGTCAG
 TCATTACAAGTGGATTCACTACAAACCGGTAGTTCTACTGGGTTAAC
 TATGCCCTACTGTCAACAGGCACATACACATACAGACAGACAGGAAGGCA

FIG. 3 (49 of 52)

CAGAGACAAGGCAGAGC .. TGATAAGAAGGTGACCTGGGCTCTAGCTCT ..
 GCCTATCACCTAGTAAAATATTAGTTAAGTAGCCATGAGTAACTCACCTTA
 ACTTACACAGGCTCATTCTTATCTGTAAAATAGGAACATTGAAACA
 GCTAATCCCCAAGGTTGTGGATAATCAGAATTACAAAGATCAATGACAT
 TTCTATGAGAGAAACATATTCCAAGTATTGATGGAGTACATCAGACAC
 AAAGGAAAGGAAACTGAATATTGAGGTTTTTTTACCAAGAAA
 TTCACATTGTTAAATTTCAGAACTACCTCTGAGGAAAGTAGCTG
 CA^ECCATTAGAAATGATAGAAAACATCAATCTGCTGATTCCAAGGCAA
 GTTCTGCTACAACGAGAAATGAAACAACACTGGATCCCTACAGATGCAGAG
 ACCTGGGCCCCACAAATGTGAATTCTGTTCCCTACCGAATAGAGTTACA
 GTTCCATAATACAGTACTCCCTCACTTCCACAGTCTCACATTCCACAG
 TTTCAGTTACCCACAGTCAGTCAGTCAGTCAAAATATTATGAAAAATT
 CAAAAATAAACAAATTCAAGAAGTTAAATTGTCGCTCATTCTGAGTAGCG
 TGATAAAATCTGTGCCACCATCCCACCTGTCAGCTTATCGTTAGTCAT
 TGACATCGTCTGCTCCTGACATCCAACCATTGACATCATCATGACTCTAT
 GATCCAGGATCACCGAAGCAGATGACCTCCCTCTGACATATCATCAGGC
 CAATATCAGCTAAACACTGCATCACTATGCCACATCAGTCACCTCACT
 TCATCTCATCAAGGAGGCAATGGATCACCTCACATCATCACAAGAAGAAG
 AGTGGGTATAGAACATAAGATAATTGGGGCAGGCATGGTGGCTCACG
 CTTGTAATCCAATACTTTGGGAGGCCAAGGCAGGAGGATCCCTGGGCC
 CAGGCATTCAAAACCAGGCTGGAAACATAGTGAGACCTGCTCTG
 AAAAAAAATAAACAAAATTATCCAGATACAGTGGTGCATGCCCTGGTC
 CCAGCTACTCAGGAGGCTAAAGTGGGAGGATCACTGGTCCAGGAGGTC
 GAGGCAGCAGTAAGCTGTGATCGTCCACTGCACTCCAGCCTGGCAATA
 AAGTGAGACCCCTGTCTAAAAAAAAAGGTAAATTGAGAAAGAGACCAC
 ATTCAACACTTTATTATAGTATATTGTTAGAATTGTTCTATTCATT
 ACTTATTGTTGTTAATTCTTCTTGCTAATTTTTTTTTTTG
 AGTCGGAGTTCACTCTGTTGCCAGGCTGTAGTGCAATGAGACGATCT
 CAGCTCACCGCAAATCCGCCCTCCGGGTTCAAGTGATTCTCCTGCC
 GCCTCCGAGTAGCTGGATTACAGGCGCTGCCACCATGCCAGCTAAT
 TTTGTTAGTAGAGGCCGGGTTCTCATGTTGTCAGGCTGGTCT
 CGAACTCCTGACCTCAGGTGAGGCCCTCAGCCTCTAAAGTGTGGGATTA
 CAGGCTTGAGCCACTGCCCTGGCCTTTGCTAATTATAAAATTAAAC
 ATTGTACAGGCATGTATTAATTAGGAAATCATAGACATATAGAGT
 TGGGTACTATCCACAGTTCAAGGCATTCACTGAGGGCTTGGAAACAGGCC
 CTCCCTCAGATGAGGGGGACTACTGTCACTCCTCAATCATTCTGATT
 AACCTCAACACAAATGGTTGGCCAGGTCTGCCTCTGGAGACAAATT
 GCTAAGGATTAGAGGGAAAAATGTAGTCAGTGGAAAGTCACCTCT
 GCTCCACTGGACAGCAACTTAAACCCAGGCCATGACAAGTAGAAAGGCC
 ACCCCCACCTCCTTCACACCTGGAGTATTCAAGGAGTCATCATATTCA
 GGACCAACCAGGAGCAAACCTGGAAAAACTGAGCTGCCCTGAGGAAAGCAA
 TCAGCTCCACAAGGGGCTTAAGAACAAAGCTCTGGGAGGAGTGGTGGAG
 AAGAGTTGGGACACATCAGAAATGCCATCAAATTCTAAGGGCTACCTC
 GTGGTGTAGACCTGTGCATCTCAAGGACATAAACAGATGGGATAAGCA
 GATGAGATTCACAGAGGACATCAAATATTGGCTCCCCAGAAGGGAGAAC
 ATTCTAGTAACAGAGCTGCCAGCTGCAGAGTGGACTGTTCACAAAGCA
 ACAGGTGCCCTGCCCTTGAATCACCACCTCACAGGAATGCAGTAGAG
 GGACTTAACCTCTGCCCTGAAGAAAAGGTAGGCTAGGGAAACAGCTCCA
 AAATTTTAAAGGAAGCAACATAGGCATCTACTGGGAGTTCTAAAG
 CCTTGTAAATGAAACTAAAGAGCTGGACAGGAAATGCCAAATTAAAT
 TAATAGAGCCTGTTAAGACAATGCAAGTGGATGTTAATGAAGGAATG
 AGCTTCTAGGCCCTGGATCAACCGTATTAAGCAATGCTGAGCATGGAGCCA
 ATTCTGTTCACTAGATTGCTCAGAAAGGGCAGACGAGAAGGATTTTC
 TAAAGGCACCTACTACCAAAAGCTGCCAGGGCGTCCAATGGAGGCCAGA
 GAGAATATGCTAACAAATAAAAGGTGAACACCCCTCAATAAAAGGTAA
 AAGTAATTAAATAGAAAATTACTGAAAGCTTTTGAAACCAAAAGTAGTC
 AGCATTGGTAAAAGTCTACAAAAGTGGACACTTCATATAATGTTGGCAG
 GAGGGTAAAAGACATAACCTTTGGAGGACAATTGGCAACAGAGTAC
 CAAAAACCTTACAATTGAAGAGAACTTTGCCCTGAGTGCAGTGGCTCACA
 CCTGTAATGCCAACACTITGGAAGGCCAGGTGGAGGATTGCTTGAGCC

FIG. 3 (50 of 52)

52/118

CAAAAGTTGAGACCAGCCTGGGGTAACACAGTAAGACCTCGTCTCTATG
 AAAATAAGAAAAGTTAGCTGGCATGGTGCATGTGCCTGTGGTCCAA
 CTACTTGAGAGACTGAGGCAGGGAGATCGCTTGAGCCTCGGAGGTCAAGG
 CTGCTGTGAGCCATGTTCATGCGACTGTTCTCCAGTCAGTCTGGGTGACAGAAT
 GAGACCTGTCACCAGAAAACAAGGCAAGAGAGAGAGAGAGAGAGAA
 GGAGAGAAAGAAAAGAAAGAAAGAAAGAAAGATGGAAGGAAGGAAA
 GAGAAGAAAGAAAGAAGAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAGA
 AAGAAAGAAAGAAAGAGAAAGAAAGAGAAAGAAAGGGAGAGAAAGAAGGA
 AGGAAGGAAAGAAAGCAAGCAAGCAGGAAAGGAAGGAAGGAAGGAA
 GGAAGGAAGGAAAGAAAAAGAAAGAAAGAAAGAAAGAAAGAAAGAAA
 GAAAGAAAGAAAGAAAGAGAAAGAAAAGGGAGAGGGAAAGGGAAA
 AGAAAAGGACAAAGAAAAGACCTTGAACCTGAATTTCACTTTAGAGA
 TTCATCTTAAGGAAATTCAATTCCAATAGAAATTATCCCCAGGATTATCT
 AAATATTGCTTTATTTCTTAGTAATTATGTTTAACCTTCTCA
 TGTTAAGCCTTAATTATTTGAAATTATTTGGTATGAGAAAGTGTG
 ACCTTTTTGTTTACTTTAAAAAAATGTATTACGATTATTATTTAG
 AGACAGGTCTGCTCTGTCACCCAGGCTAGAGTGCAGTGGTGTGATCAT
 AGCTCACTGCAGCCTGAACTCCTGGCCTCAAGCAATTCTCCCTCTCAA
 CTTAGGAGTAGCTGGGACCACAGGCATGTACCAACATGCCAACTAATT
 TTTTATTGTTGTTAGAGACAGAGTCTTGCTTGTGCCCAGTCTGCAAT
 GTTGTCTCAAACCTCCTGGCTCAAGTGTATCCCTGTCGCCCCAGCTCCAA
 AGCACTGGGATTACACGTGTGAGCCACTGCCAGCTGCCCTTTATT
 TTTAATTTCAGATGCTTGTGTTCCAAAATAGCACTTATTACCC
 CGCTTCCCCCTCTGGTTTAAATACTGCAAGTTGGCTTGAAATACAA
 CCCACTGCCTTATTCAAGGCTACATTCAAGGAAATCTGAGACCAAGAGTCT
 GAAGGCCAGTTCTTCTCAAACCCAGGAGGTGAAATGTGTCACCT
 CCACACTTCTATCTATTCTAAGAACTCCTTCTTCAAACCTGACAT
 GCCCTGGCTCAGGTCTATAGAAATTCCAGGGTCCACAGACAAGCAGA
 ACTCACTTATGGGAAATCTGGGAAATACTTATCTGTTAACCTGCCCA
 TATGGTGAETCAGATTGTCTAAAGCCAAAGCATCATTCTCACCCAAA
 CCATTCTCTCCAGACTCTCTATTCTGTGTCAGACTCAAGATCT
 TGATATTACCTAGAGTCCCCCTCTGCTCTGTCATACCCAGATGCC
 CTCCCTCCCCAGATCCATTCTCCACCCCTCCCTCCATCAGTTGGG
 CCCATCACCGCTTCCCCCTGGCCAGGCTCTCTTTGTGCGCTTGGAGCA
 GCAGACTGATCTCCAGCCTCACTCACTCATGTGTTAATCTGTTGT
 TCATCACTGTCAAGATCTCTGTCATCCCCTCACTACTCTGCTGAAACAC
 TCTAGTGGTTCTCATGCTATTAAAGTCTAGATAATTAAACGTAG
 AAGGCCAGCACAATTGCCCCATGCCACCTACCTCTAATCTTTCT
 CCTTACTCTGACAGACTCTCGTCTGTCTTTATGTTCTTTATTGCT
 CTCTCTACTTTAGTATGAACTGGATTATGGATTTTAAACATTGCT
 TTCAAGTATGGAATAAGAATTTTATTATTATTATTATTATTGAA
 GACTGGGTCTCACTCTGTTGCCAGGCCAGAAATGCAATGGTGCAGTCATA
 TCTCACTGTAAACCTCGAATTCTTAGGCTCAAGCCATCCTGCCCTCAGC
 CTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGCTAATGG
 AATAAAATATTACAATGCCATTCTAATTCTAAATTCTAAATTACAT
 TGTACCTAATGCCATGCTTACTTTCTAGTGGGCTAATAGCCCTCA
 CTTGGCAAAGGTCCCAGGCCAAGGTAAAGGCCCTACTTTCCAAACTC
 ATCTTTGAAAGACATAAGTGCCTGTAAGTTGTCACCACTAGGTTCTAG
 GAATTCTCATCAAAGACTTTATCAGACTATTCTCTAAGTTGAGAAA
 GAGCTGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCACTGAAA
 TCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAGCAATGA
 GGAGCCGGTGTGATGATTGGCTTCAAGGGAGGTGTGTCACACACCGATT
 TTATCTACGTGGATGAAACCACAGCTGTCGGCTCCCTGTCTCCAGGAC
 ATCACACTCTCCACATTCCCTCCCATCTCCGGCTCTGCTTCCGGGGC
 CCTCATCTGCCCATCTGGGTGAAACACTGGTGGTCAACTGCTGGCGT
 ACCTTCCCGCTCTGCACACCCCTGCCACCCACTCTCACGGC
 TCGCACTGCAGAGGAGGCCATCTCTAGCTCCAGCCCATCTGCCCTTCT
 GAGCTCTAAACTCATGTAAGGCAGACTCTGCCGGTGTGTCCTCACAGGCC
 ATCATACTTCAAAGCATTTCCCTCAGAACACCATGTCCTGGCTGCTCC
 CTCCAGAAGATACATCTCTCAAGCACATCCCCGGCTCACCTGGATG

FIG. 3 (51 of 52)

ACTGCATTCACCTTCTC ACATTGCCCTCCCTGGATGTATAGA.
 GTTTAAAATACAAATCTGATGTGCTTCCTGCTTGAAACACCTCA
 AAACCTGCCCTCAGGATAAACCACTGCCCTGACATGTTACAGGTTGCC
 ATGGCCTGGCCCTGCCCATCTCTTCAGCCTCATCTCATGCCCTGCC
 TCGCTCTCTGGCTCTGCCTCCCTAGCCCTCCTTAGGTTCTAACAC
 ACCATAGTCCTCTAGTGTGGGCCCTGCAGTGTGTTCCCATTGCC
 TGAGACATGAATCCCTCCCTATCTACCTGCACCTCATCTGATTAA
 TCCCTACCCCTCCTACTCATGATGTTGCTTCAGGGACTCTCTGAC
 TTTTAAACTAATCAGGGCTCCCAGTATATATCTTCATAGCACTGT
 ATTACTCCTTCTTAATGACCACCTGCTGTAGACTGAATGTTGCTTCC
 TCCAAAATTATCATATGTTAAAACCTAGCCCCAAATGTGATAATATTGGAG
 GAAGGCTCTTGGGAGGCAGAGCCCTCATGAATGGGATTAGTAGCCTTAT
 AAAAGAGACCCCTGAGGGCTCCCTGTCCCTCCACCGTGTAAAGGATGCA
 ACAAGAAAAGTATGGTCTATGATCCAAAAGCAGACCCCTGCCAGGTACCC
 AATATGCTGGCACTTGAACCTCCCAGCCTCCAGAACTGTGAGAAATAAT
 TTCTATTTCTAAGCACCAGCTATGGTATTTGTTAGGAGCAC
 AACAGACTGATGTGCCACCCAAACATGATTATACGTGTAATTATGGTT
 TCTCTGCTAGTAGGGATGCACCATGGGTTAGGAACCAAGCTTCTTAT
 TTCCACACAGCCTTAGCTCTAACGATGTTCTGAATCAAAGATCCCA
 TCTTTATGAATGAAGGAGTCAGTGAATGAATTAAATGAAAGAACTGATAA
 CCCTCAATAATTATTCAGCCTTTATACCTACTATTAAACAAGCTTGCAT
 TCTACTCCAAATTATGGGCTTTAACTCTATTGCCCCAGCACATT
 GACATCCCTGAAGTAAATCTATGCTTCCATCTAACGTCAAGGAAGGAC
 CTGGACTAGTAGGGCAAGAAAGGTCTAAATTCCATGGGTGGAGAGAGA
 GACTAAATCTGAAAGGAAGAATAGATTGAGCAAAGGTGTAGAGATTGGGG
 AAGGCTGGACATTGGAGAGAAGGAAAGGAAACTGACACTAAACCAAC
 AGTCTCACAAACACAATCTCATCCCTCCAAAACCTCTGTGAAGTAAGAATT
 ACTATCCCAGGGCCAGGCACAGTGGCCCATGCCTGTAATCCCAGCCTT
 GGGAGGCCAAGGTGGTGGATCACCTGAAGTCAGGAGTTCAAGACCAACC
 TGATCAACATGGTGAACCCATCTCTACTAAAAATACAAATTAGCTGG
 GCATGGTGTGCACACCTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGG
 AGAATCATTTGAACCTGGGAGGTGGAGGTTGCAAGTGAGCAGAGATGTG
 CACTGCACTCCAGCCTGGGTGACAGGGAGACTCCGTCTCAAAAAAAAA
 AACAAAAAAAAACCAAAAAAAACAAAAACAAGAATTACTATCCCAG
 TTTGAGATGAGGCAATGGAAGCTCTAAAAGTTAAGTAGGAGAAACAA
 ACATGAAATGTATGTCTATGCTTTCTCATCTTCTCATGCTGGCTGG
 AATGTCCTTCTCCCTCACTATGCAAATCTAACTCTCAAGCTAACACA
 TAGCAATGTCTGAGAAACCGTCCCTGTGTTCACTCTGTGTTAGCCTCACTG
 CTCCCTCCCCATCCCTCTGTTCTTCTGTTATAACACTCTCTATTCT
 GCTGGCATCACAGTCATCTCACCTGCCTTCTCACAAGTTAAAGCTT
 TTAAGGCAAGTGGTCTTGCACCTCATTCCCCAGGGCTCTAAC
 CAGTCCTCATGCATGACAGAGTTGAAAACAGGTTACCAAGCTGGCTTC
 AGGCAGGTTGCATGGAACTGTGCTTACAGGAATACCTGCTCCCCCAG
 GCCCTGGGTCTCCTCGAGTCAGGCTCAGACTCTCATCTGCTCG
 TTCTCTCTGGGAGCCACAGTAACCTTGAGCAACTTGCATGGATAGA
 ATGGCCTATTAGGGCAGCACAAAGACCCATGGAGGGAAGAGTACAGAA
 AGGGAAAACGATAATCATATTTTTAAGATGTGCAATTCTTAACAAAA
 TGCTCTAGTACTGTCCAGACTTCAAACCTAAACCTAAGCGTCTT
 TCTTGAGATCATCAAAGGCCAGTGGTCTTCAGGTATGTCAAGCTT
 CTAGAAAATAAGGTAAGTCATAACTTAAACACACATGGCTAAATGGC
 CATTCTCTAATTATCAGCACTGTTACATATTCTATACTAGAAAA
 AATTATATTATACTCAGGGTGGTAAGTTAAATTGCCATGAAGTAAA
 GCAGAAAGAGCGTAGCATGTATGTATGTAACTCAACTGTGCATGAGAC
 AAAGATGTCTGAGGAGAATGAGTCTAAGATGCGCCTGAGCAATAGTACC
 C

FIG. 3 (52 of 52)

54/118

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GCACCCATTTCTAAAGGGCATACCAGCCATAATAACAGGAATGGGTGAG
 GATATAGACAGCAGATGACAGAGAGGGAGTGAAGCTGGGAATCCCAGC
 TAAAGGCATCAGGTTATGGAATGAGTAGGGGACAATACTGTGTGT
 ATACACACATGTATATGTGTATATGTATACATGTTATGTATATAT
 AATTATATGGTACCATTTCTAATTGACAAAATAATCTATCACATTTACA
 TTATCAGATTTACATCTATTGTTCTAAATACACTCAGTCATCAGCCCTG
 TGTGTGGGCTCTACCCATCCCCATGACACACTCAGCTCAACCACTGATG
 GATGGATCATCTGCCTATCAGAGGTGGCATATTCAAGGTGAATCCATGGCC
 ACAGCTGCAGCACTTCTACCCACGCAGAAAGGCTCCAAGAGGGAGGCA
 CACCCGCTCTGACTGTCCTAAGCTCCTGACATCTCACCCATGAAACT
 GCTGTCCTGGGTGTTCTGCCCTGCCAACCCCTGTACTGTTCT
 CACCAATTGACACAGCTGGTGCCCGATGCAC

>Contig2

NAAAACGAATCGTCACTATTGAAGCCTGTCCTCANCGGATCGTACTAA
 GAACCCCCCTCCTTGCTTCAGTTGTCCTGCCCTTCTAGGCAGAGCCACCC
 TACATCTTAAATATATTGATTGATGACTTACGTCTCCCTAAAATATATAA
 AACCAAGCTGTGCTCTTACCAACTTGGGCACATGTGGTCAAGACCTCCTG
 ATGCTCTTGTATGAGTGGGTGGGTCTCAACCTGGAAAAATAAACT
 TTCTAAATTAACTGAGACCTGGGTCAAGATTTTGGGGTCAACAGCAACAA
 TTTAAAAAAACTCACCATGACCTGAAATTGGACCTTATGCTGTTCTCA
 CACTCCTCCATGAAAATAGACGCCATCCTATGAGTCCCTCAGCCATGTC
 ATGCCACACTTCAACATGTGTCCCCATCCACCATCTGCTTCTTATTGC
 TGCACTCCTACCCAGGCCCTGATCTCTGGACCCATTGTTGATAATTAGA
 ATTTGGGGCTGGCATCGTGGCTGGCTCACTCTGTATCTAACATT
 TTGGGAAGGTGATTAGTCAGGATTCCCTCCGAAGGATGCAACCCCTAGGGA
 TCCTCTCTATGACCCATGTC

>Contig3

CGCGCTCAACCGACCGATTGGCGAACCTGCCCATGCCCGAGGACAGTG
 TAATCCTAAACGTCCTCTGAATCATAGGATATGAGTGCAGAAAGTACGG
 TTCCCTCTGTCAACCCTTCTAACAACGCTATGTCGATCCGTGCACTAA
 CCCCGCCCAAGTCAGAACACTGATGGCGCTCCCTACAGGTATCC
 AGGGCCAATACCAACTACTCCCCTCTCCCTCCACTCTCTAG
 AGGCCCGGGATGCCATCCTCTATTAGCACAACGAAAACGACGGTGAAG
 TACACAGCTCACGATCTGATGGTGGCCCAATGCGGTTACAACGGCT
 GTCATCCCAACCCCCGTCCCATCTCCATTTGCCCCCTATGAGGAT
 GGCCCTATCATCATGACCTCCAAAATTCTGTCATCTCCGACGTAATGCC
 GCCCTCGAACGCCCTGACACCATCAAGTCNGTCACCTCCAAAATACTCC
 TCCTAATCACCAAGGCCGAGTATCCCCGGTCCACAATACCTCCTGAGAC
 GGGCGATATCACACAC

>Contig4

NGGAGTTTAGGTCAACTAGTAACAAGTGGGATTGCGACTCAGGTCTATC
 TAATCCTCAAACCCACGTCTGGACCCCTAACAGACTGCCCTCCCTCAG
 TCCTCTGTGTGGCCTCAAGAAGGGTCTGGACATTCAAGTTAAAATCCA
 TCCAAAGAATCTATGGACCCAGTGGTCTCTGGAGTCATGTTCTGAGGCT
 CAGAAGGGCCAGGCAGGAGGGAGCCGCTCTACACAGTCCTGAGCAGAGT
 GGGCTGTGTCCCGGCACAGCAGGGAGATCATAAACAGAATTCTGCCCTG
 GGCCCTATTTAAGTAGGACCTTTAGGCTGCGGTGTCATGACCACAGGTC
 CCANGCTGACGATTGGCTGTGTGGAAAATCTCACTCCTTGCGGCC
 TTGTCCTTGGCAGAGGAGACCGCTGCTTCTGATGGCCACCAAGGGG
 GGCCTCCCTGGAACGGTTGAANGGGAGCCTACCCACACGTGCCT
 TCCGGTGTACCCAGCACCAGTCGTAACCATGGTTACCCACAGGCCAGC
 TCTGCTCTGAAGAAGGAGGAGTGGTGGCATTGACGCTCTGCTGATCCC
 GTGGCTGCCCTTCTTTCTT

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GGGAGCTAACCGCTCACTGGGATTACAGGTACGCACCACGCCCTGGCT
 AATTGTATTTAGTAGAGACGGGTTCTCCGTGTTGGTAAGGCTGG
 TCTCGAACTCCAACCTCAGTTGATCTGCCCGCTCAGCCTCCAAAGTG
 CTGGGATAACAGGTGTGAGCTACCATGCCTGGCTTATATGTTCTAGTC
 CAAACATTAGCTACCTTTTTTTGAGACGAAGTCTCACTCTG

TGCCCAAGCTGGAGCACAGTGGACAATCGTGGCTGCTGCAGCCTAAC
 CTCCTCAGGCTCAGGTGATTCTCCACCTCGGCCTCCCTAGTAGCTGGGA
 CTACAGGTACGCCACTACACCCCTGCTAATTTTTGTGTTGTTGATTT
 TTGTAACAGATGGGTTCTCATGTTACCCANGCTGGCTTGAACTCCTG
 GGCTCAAGCAATCTGCCACTTCAGCCTCCCAAAGTGTAGGATTACAAG
 CATAAGCCACCATACCCGGCTACCTACTTTAACCTGTGGAATTCTA
 TAAGGTCAANGATGCCCTNGGGAAACAAAAGTTCTCCCTGGTATATGCA
 AGTAAAATCCACATGCTGCCCTCC

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AGGACTGTAGCTGTTCTAGTCACCAGGCTGGACTGCTGGCATGATCT
 CAGCTCACTACAAACCTCCACCTCTGGGTTCAAGGGATTCTCCTGCTTCA
 GCCTCCAAGTAGCTGGGATTACAGGCATGCACTACCATGCCCGCTAAT
 TTTGTTATTCTTAGTGTAGAGACGGGGTTTCGCCATGTTGCCAGGCTGCTCT
 CAAACTCCTGCCCTCAAGTGTATCTGCCTGCCCTCCCAAAGTGTGCTG
 GGATTACAGGCCTGAGCCCCGGCCCACATGTAAGTTATATCTCTGT
 TGTTTACACCTGTTTTGACCTAGTCTTCAGTGATTGAATCTTGATTC
 AGTCTTTGTTATTAGTGGTACTTCCAGCTTGTGTCATCTGTGGAT
 GACATATGAGTCTTGCTCTTCATGCCATTAAAGAAAGACTGAACGGGAA
 TAGGTCAAAGGCATGCCATGAGCGATTCTCCAGCTTTCATGGTGT
 TCAGCTCAAATCTATTACATATTGGACCTGCAAGCCATCATCTTATCC
 ACAGGCTATCATAGGTGAATGAAATTGGGTTAGGTGGCCAAGCTG
 AACGTGAGATATNTTC

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AGCATGTTCTAAAGGCCTATCAAAGCTGACATCAAAGGGATAAGTTCC
 AGTTACCCAGCTGAAGGGAAAGGAGGGTGTTCAGATAGAGGAAGGATAAG
 CATGACCTATTCAAGGCAGTGAAAGAACGCTGCAACGCCAAGTCAGGA
 GAACCTGAAATTGTGTCAAAGAGCTTGGATGCAAAGAGGCCGTGGAGACT
 ATTGGGGGTTTAAGCAGGGATATAATATTCAAGCATGCACTGAGTAAAA
 GGTCACTGGCACCTGCCATGGCCAGGACTCGGGCTCTACATGATTGCGT
 CTGTTTGGAAATATCACCCCTGGCTGTGAGATGAAGAACAGGTAGGAGGG
 TCACAAAACCTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTGTG
 TGGACTGTGCAATCACAGAGGCAGAGGATATAATGCACAGAGACACAA
 GGCATGTGGAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGG
 GTTAAATGGTGAGTGANAAAGACATACTCAAGGTGACACGCCAGGTAT
 CTGGGTGGATGGTAAGACATTCACTGGACTAGAATCGAAGAGGAGGTGGGG
 ATGGACATTCTCCGTTAGAGGGGTTACCAGGAGGATTGCCGGAAC
 ATGGAGAGGATTAACCAGGAATCCGGTGCCTTTCCAAACTGGGTTGGA
 GGGG

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GGTGAATGCTTGGCACGCTGTGTTAGGTGACGGGTGGTACAA
 TGAGTCCTGTCAGCGCTGATTTCGGCTTGTAGAGCGAGATTATA
 CAATAGAATTGGCATGAGATTGGATTGCTTTAGTCAGCCTTATAGC
 CTAAAGTCTTGAGTGACTAGATGACATATCATGTAAGTTGCTGATAGGT
 TTCCAGTTCCGCTCTAGGTCTGCATATTGTACTTTCTCTTACTCC
 ACTTAACCAGTACCAACCCAGCTCTCAACGGATTATACCATGGCACTT
 TAAAGCCAGCATCACTGACAATGAGCGGTGGTGTACTCGGTAGAATG
 CTCGCAAGGTGGCTAAAATTGGCATGAGCTTCTTGAACATTGCTCT
 GAAAACGGGAACGCTTCTATAAAAGAGTAACAGAACGACCGTGTAGTGC
 GAATGAAGCTGCCATACCATAAAGTCGTTTGCTCCGAATATCAGACC
 AGTCAACAAGTGTCAATGGCTCGTATTGCCGAACAGATTAAGCTAGCA
 TGCCAACGGATAAACCGAGTCGCTTGGTGGAGGG

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GGGGTGGGGCGCTGGTGTCTAAAGAGGATCTCTGCCAGAAATGGTG
 TGCTGACACTGTTGCTCTTGGTGTGGAACCTTGTTGTTGAAAGAAAGGT
 TGGAAAGGGAAATTGATCCTGGATTAAACCGAGTTGTTACTGATG
 CTCAACAAGACTAGGGAAAGGATAAAGGCAGGTGAGTCACTCTAGGATGGC
 TCANTGAGCTCCACAGAGCTGGAACACAGGCACCCAGGAGGGATTAGAG
 CAGGCCTCAGTCAGCTGAGTGAACCAATGAGCAGGTGATGGGTC
 CAGGCAGAGCCCTGTCCTTTAGGCAAAACCCCTGAAACACCCTG
 ATCCTAGCCTGTTCCACCCAAAGCTGGCAGTCTCCAGGCCCTGCC

AGCCCCAAGGAAGTGGTATGGTAAAACAGAAGGGCCATTCCGTCCAATG
 TGTGAGGAACCTTCATTCAAGACTTGGAGGCCCTGATGTTCAAAACC
 TCAATGATATCATTCAATTTCCCCATCCATCAATGCCCATCCAATGCC
 ATCCGTTCAATGCCCTCCATTCCCTTCAGGGAAATGAAAATTGTTCA
 GAAAATCCTTCTCTTCCAGAAACCAACCAAACCGCGAAATTCA
 CTAAACTAGCCAAGACACAATCCTGGGTATTTCCCTTCCAAACCTC
 CTGTGTTAAATTAAATTCTACCCCTGGGTCTCGGCCCTACTGCGAAGGTG
 AACTCACCTAACCTCTCCAAACAGAGAAGAAAATTCTCTGGTAAAATG
 GGTTTAACACTTCTAAAAACCCCC

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GCTATGGTCTAAAGGTAATGGACTATGGCGTACACAACGTCTCGCTCAT
 CGTCTGCCAGGAGGCTAAGGTATCCACGGACAATCGCTGAGCAACAGTGT
 CGTTGATCCATCTCTGTAACGCACTTGTCAACATGGCAGGAGTACGGGAGC
 TGCAGAGAATCCTCTGCTGATGTCACGGAGCATGCCGTGAGACAACG
 CCACGAACGGCCCTCGGAGANANCTACTCTGCAATGAAGACGTACGATAC
 ACACGTAGGAGTCTAGCTACCCAGCGTATCTAGGTATACTGTACTCGC
 GGATACTCACTCGTGCATGCGGCAATAGATCGATACGCAGTCGTACGCC
 CATGCTCTCAGTGTGTGACCTCTGGCGTAGCGTNGTGGCGCTATTAC
 TGTGCGCAGCAGCGCAGCTGACATGTGTGGTAGCGATGCCAGGAGCT
 GTAACATAGCAAGTCGCCCTACTCCTATCACTATCCCTACGCTGGAC
 CGCACTCGAGAGATCTGAACGCACGCTTAACCTGCCAGTACTCGTGAGACC
 TATACTGCGCAAGCCTGGCTAGGAGATCCTGCAGGCCGGAAAGAACATC
 AGCTATGATCCCCTTGCGATTATCGCACACGACCATAAGAGTATGTGCAT
 ATTAACCTCTGAATGTGCTGCAAGCAGACGTTGCTCAACATATATATGG
 ATGTGGGAAATGCCCTGGTACCGCCACTGGCGTCAGGAGGCACCAG
 CACGTCTGAGTGTACGCACGTTACTC

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GGCGGAATGGTAATTCACTCGTGTCTCGAGGGGGTGAAGACGGGGAG
 TTATGCTGAAATGGCACCGCTCACCCCTGGGTTATGAGCAGACCTAACCC
 TCCCAGTGTGGATTACAGGCATGAGCCACCGTGCCTGGCCAGTAT
 CTGAACCTCTGTGGCCAGGCAGAAAAGGTCTGTGTTACTCGTCTCCTT
 ATCATTCACTGCCATATTCTCCATTGCTAACATTATGTTCTGCTCC
 ACTGGATTCTTGGATTTCAGAACATACCCATGCTTGCATTGCCCTT
 GGTCTTGAATATTGGTCACTTCTGCAAAGTCCCTCTCACCTTA
 TCTTCTGGTAAACTCCAGCAACACCTCTTACTAACCAAGAGAAACAT
 GGTCACACTGTGCACAGGCTTGACAGAAACTGTTCTCATATTGTCTGT
 CATTGTCATGTGGCAGAGATGCACCTTAGATACTCTTGGAGAAAGGAC
 TCACTGCCAGCTGCCCTGGCACGTGATGAGCTGATAGCTCAGCTATAGA
 CTCTTCTGGTCAACCTCTGCTTCCAGTTGAGATCATATCCTTGCAG
 GGTGGCCTCCCCAGTGTGACTAAGGAGTGTACAATGGCCTAGTCATT
 TCCTCCAAATGCTGGACTCCAAATGAACCATGCTCCGGAGCTTCCAC
 TGGCAGTCAGAGACCTTAGCTAGTCTGCCCTGAATCAGAAGGCTCT
 CTTGCCACTCTGGCC

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GCTGTGTCTAAAGATTACGGCTGTAGTTCAACTCCGCCGCCCTTAC
 TGTGCTCTTAAATGGCAGTCATTCAACCATCTTCTGTCCCTCCCTCA
 TTTCTGGATGGTACTGTCACTTGTGCAACAGAACCTGTCCCAATC
 CTTGATGGTTCAATACACACATAGACATTCTTTAACAGGGGGCCTCT
 CAGGTCTTAATTCTCCCTCAATAACCTTGTGATGATCCCCAGCT
 TAGCCACTTACTGCCAGATCATTACAGTAACCTCCAGGCCCTCTTAATT
 CTAGTTCTAATATCCTAATCTGTGACCTCACATTCAACTTCTCATTC
 TTATCCCTGAGTCAAAAATCCTTGTGATCCATGCAATCCATTAGTCAT
 CTACCTTCTAACCATCTCGCCCACTAGGGTTCTCATTCCTTATTAC
 CCATATGAAATTCCAAGGGCTGTGGAATCAGTCCCTGAGCCACTGTC
 AATACTCTGCCCTTTACTTCATCACCCCTATGTGGCAAACACACAGC
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 ATGGCTGATGGAGGTTGGAAAAATCCACACATGCAGTGGGCCCTGTATGT
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 TACAAAATTAGCTGGCGTTGTGCATGCCTGTAATCCCAGCTACTCGGGA
 GGCTGAGGCAGGAGAATTGCTTGAAACCGGGAGGCAGAGGTTGCAGTGAG
 CCGAGATCACACCATTGCACTCCAGCCTGGGCAACAAGAGTGAACCTCA
 TCTCAAAAAAAAAAAAAAAATTAAAACCTCTGGAAGTTGAGTTG
 CAAATATTCAATTGCTCATTTTAACTTGTATGTTGGAAAATGTCATG
 ATGAAAATTGAGGTTGGGGATGAGAAAAAAAGAAAAACATCAACCCAC
 AGCCCATTCAATTTCAGCCCAGCCACAGCTCCGGGAAGGGCAGCAGG
 TCCATCCTTCACTCTTCTCACCTCTTCCCCCTCTTGTGCTCTCCA
 CCTCTAATTGGAGCCAAAAAAAGGCAGTGGAAATGAAAAGTCTTT
 GTACGTGGTACTTGCCTGGGAAGCTGCCATGAAAACCTGGCCCACGGTG
 GGGAGGGAAATGCCANCTGAGGCCTCGTGCCTAGCTAGGATAGACTCGT
 CCAAAACATGTCAAGGTGGCTGACAGGGCAAGCANCANGAAATCATGTATG
 AGTATGAACCTGATCTGTATGCAAGGGGGAGAACACGGGAGGAATGG
 GGCCTGAGAAAACAGCACAGTACGTTCTTAGCAGCTGCTCTGCTCAG
 CCATGGGAGGTACAGAGAAAGAGGCTTGGAGGCGTTATTTCACTGTGA
 GATGTGAGTGTAAAAAGTCCAAAGACACAGTGAAGTACCGGGAGATGC
 CCTCTTCCCTACCGAATGCAAGAACAGGCTTAAAACACACACA
 TGGGTCTCAGAGGAGAGAGGGCTCCACAGTGGACACCCGCATTCTCCCC
 TGGTCAGCAGCAGCAGGGCAGTGCCTGGGCATCATGAAGCTTACAGGC
 AATGAGCTCTCAGCAATAACAGGAACAGTGCCTGGGGACTGTAGCTGCA
 AGACCGATTTCATGTAAGATGGCTCTGAGGACTCCAGATAACCCAGG
 CTGAGACTAGCTGCAGCTCAAGTTGTTAGTACATCCCTTACATCCGACAACCA
 AGGGAAATTGAAATTACTGTTACTACAATTCCCTTACATCCGACAACCA
 TGAGGTCCAGCATTCTATTATTTTTTAAAGACAGGGTCTCAGT
 ATGTCGCCAGCATAGAGTGCATTGATGTACATGGTCAGTACAGTAT
 TCACGTCCCAGGCTCAAGTGCACCTCCTGCCTCAGCCTCTCAAGTGGCTG
 GGACAGCAGTTGCATGCTACCAGGCCAGGTTTTTTTTTTA
 GTTTCTGTAGAGCACATAGC

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GGTTAACAAATGGCACAGGGAAACAAACAGTCCAGGTGCAGGGCTCTAA
 ATCTATCATAAGATGTTAGGTATGGGGCTCTGCCGACACAAACTCAAG
 GCTTATGCTGTTATCTCTGAGCGAAATCTGGAACTCGTACATTGC
 TTGCTTCAGTACCTTATCAGTTAACGGACTCTTGTATGTTGGAGTC
 AGCGTACACAAGTTAACCTTGAGGAAGGGGGTGGGTAAAGGAGTCCTTG
 ATGTCGGTAAATGAAGGAGCGAAATCGAGTTCTCTGGCTTCTCAGCT
 AAGGGAGAGCTTATTGTTAAAGGCTAACAGGCTAACAGTGAATTAGGGAGAA
 GGGAGAGTCTGAAAACAAGGTTAGGTATTACAATGTCAATAAAATTGGTC
 TCCTTATACAGTCTATGGTAGATTCTTCCATCTTAAATCTCCCTCTA
 GCACCAACCAGACTTTCTCTGTACCTTGAGATGTAATTGGCTATC
 TGAATTTCGCTTAAGAGTTCTTAAATATGCAAATTAGGGTTAT
 TTAGCTGACAATGCCAAAGTAGTGAACAAAGTTACAGAACTTGAACG
 TCTAAGGTAGGAAAAAAAGTCTTATGAATCTATAAGATGTACTTCT
 ATTGGCATGCCATAACGTCTATGTATTACAGTGTGTCACAGTTT
 TCACTACTGAAAATATAGAGGGAGTCTAATTAAATTGACTTAAGACAAT
 AAAAGCGCTGAAATCAAATACCTTATCAGGAAAAGGAAAAGACAAGTCA
 AATGCTTGTCAAGTTATATAACTTAAGTAAAATCTTAATAAAATAAGC
 TAGCTTAAACATTATTTGAAATGTCTTAAGAATTGCCAGCAGGTTCTGGG
 TTACAGAACTAGTGGGGGTGCAGTGGGGTGGGTGGGGTGGGGGG
 TGGTACGGGGGCTTGTGTTCTGCTGCCCTCTGGTTGGGAAG
 TGGCAGGACCTTGGCAGCACCCGAGCCGGATGGCTTAATAATGGAGG
 GATGCCAGACCCAAGTGGCTAAGGCCGGCTGCAGGCCAAGTGGCATT

FIG. 4 (10 of 61)

64/118

TCCAGACTGGGCTCGGGCGCACCTCTCCAGGACCTCCCTGTACC
 GAGCAGATTGTCGCGGGCAGTTGGGCCAGCTGCTCTGGCGTGGAAATTC
 CCAAATTCAACAAATCCTCAAGAAATCAATCCATCCATTCACTCCA
 TCCATCCATCCATCCATCCATCCATCCATCCGCGAGATTATGAAGCAT
 GGATCATTACTTTGGGATGTGGATATATTCAAGTTAACAGAGCAGCTT
 TCAAGAGCTGGATTTATGCTTGGGTGAAGTTAGAAACACTAGCTCCC
 AC_t

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ACCTCATGTGCTCTAGGCCTCTTACCTCATGCCCTCACTCTCAGTCTT
 GCACTCACCTGCCACACTCAAGGGCTTCCCCAGGTTCTTAGATTC
 CACCGATAGCTCAGGGACTTGCACATGCTACGGTCTGCCTGGCTCCT
 CCCCCAGATCTCTCATGCCCTAGCTGCTTCTCATCAGCACCCCTCAGAGAC
 TGTCCCTGCCACCTCTCAGGTTCCATACCTGCCACCCCTCCCCAATC
 ACGTAACAGTTCTCACAGAGCGAGTTACCATCCCAGTATTCCTAAC
 TTATTTTTGTGACTGGCTGTTGCTGTCTCCACCACAAGAACATAAGC
 TGCATGTGAACAGGAGCCTGCTATCTGTCACCCAGTGGCTGTGACA
 TAACCTGATAACATTAAGATGCTCAATGATGTTGATGAATGAAGTGCTG
 GTAGTCCAACGTGTTCTTGTCTGTGAAGTATGTCGTTGTGGTTTC
 CTAAGAACCTACAGCTCTCCACTGTGACTCTGCTATGGCTCTGATT
 TGCTGGACTAGAACCTAACATGCTTACTCTTAGTGTCTCCCCA
 GAGGCTGAATCCCAGTCCCTAAACCTCACCACAGTGGCTAACACTAGCT
 TCCAACAGACAGGCTACGCTGAGACCTCAGCACGCCCTCTGCGGTC
 TCATCCTTAACGCATCCTCAGGGCCAGCTAAATGTCCTCTCCAAG
 GAAGGCTATCCTCTTCTGCCCCAGTGTCTCCATGCCCTCTATGC
 CTCCATGCCCTCTTCCAACCTCAGAGGGTGGAGAAGTTGCTAATCTGC
 TGTGTCATGCTGGCTGGCTGTGCCCCAGGTCCATGCTCACTCCTGAGCCCC
 AGTGGAGTAGGGCTCCCTTCCCTTATTGCACTCAGAGGAAGGACGTG
 CTTCTTAGGACAGATCTGCCAACCTCTCCCTCGTAGAGAGAACGGCCAGC
 CATCCTCTGCCCTCTTCTCTGCCCCAGTAATAAGGTGCCT
 GGTCAAGAGCCTCTAGAAGGAGACCCAAACATCCACACACATTCCCAGT
 TCCAACCGTCATCCACATGGCTGGCTGTGCAAGTAAACGCAAGACTGTT
 TCACACACCCAAACCATCTAGTATTGGATGGGAGGACAGTAGCGTGA
 CACTCTCCAGCCTTGAGCCTACTGTGGGCCCCACCAACCCAGATACCAG
 AGGAGCCTGTACTGGGATGCTATTGGATGCTTGTCCAGTCATGTACAAA
 GTTAGCCCTTGTATATAGAGTTAGCTACGTACATCTCCTCTGTAGGG
 AACCCAAAGAGGGAGAAGAGATATGAGTAGGATTAACCTGCAAATCCT
 CTGCTGAGCACCGTGCACATACAGTGGTAGCATGTGGTAGGTGCTC
 AATAACTATTGACCGATCTATTGAATACACGTAAGATCGTACACTATCT
 AAAACGNGGGGTGTGGGGAAAAACCCCCCTTGTAGGAAACCCAAA
 TTGGACCGTGTGGC

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GCGCGATTGTCATAAGATCATGCATGCCGTACAAACGTCCCCATATGG
 CGTCAGAGTCACCTCTCCCCATCAGGCCCTGACTCGGCATAACA
 AACCTGGCAGGTTAAGTATTAATCGGTCTGTACAACTGTAGCCCTTAG
 CAGGAAGCACTAACGCTCGTTTCAATTATTCTCCCTGGAACTGCAAG
 AAATGAGGGATGCCCTCCGCCATGAAGTTTGCTGATTGTCCACTTGT
 CTCAAGGAGATATTACAGTTTAAATTGTCCTCTCCTGCATGGTC
 TCCAAACCTGTCAAAGAACGCCAGCTGGCTCCATCATGTAAAATCACC
 ATTGTCAACCAGAGCACTGACTCTCTGTTGCCCTACAAATCCACCTGCACT
 TTATTCCTGCCACCATGATAATGAGTGTACTACATTACATTCA
 TGTAAGAAATGTTACATTCACTTAAATCAAATTAGTCTGCTCACT
 CAGTCCCCACAGTGCACCAACTTATAAAAGAGAAGGGTACATTCA
 CACTGAGGTTCTCTTACCACTGGAAAATGAGGAAGGGTCTGGAGTCCA
 CAGTGGTTAACATCATTGCCCTGTTTCTCTCACTCAATGTAACCAT
 CCAAGGTTACTCACAAATTCAACAAAAGAGGTCTTCACCTCTGCTCTCAA
 GACCCAGAGGGCTGGGTTCTAAACTCAAGGCCAATGTTCCCCAACTTTT
 TGCATTGTTCAACATTGGGAAAATCGAGGGGATTCAAGAATGGTTAT
 ATAAGTTTGTGGAAAATGTATAATTAAATTAAATACAAAGTA
 TTATGGAAAGCACTAAATATTGAATTATATAAATATTCAAATATT

CTAATTTTACTGAGAAACTTGAGCTGCTCTGTGAGATATTATTT
 AAAACAGATTGACACTAAAATGTCTAATCAAGCCTTTAACCATGAT
 CTATCTTCAAATTCTCAGATGCCACCATCAATAAAGAAACTTGTTC
 ACACAAGTAAGGGTAGAAATGGCAGGGTGTATCATTTTTTTT
 CTTTTTGAGACGGAGTCGCTCTGTCGCCAGGCTGGAGTGCAGTGG
 CGCGATCTCAGCTCACTGCAAGTTCCACCTGCTGGGTCACGCCCTCTC
 CTSCCTCAGCCCTCCGAGTAGCTGGGACTACAGGCACCTGCCACCAGCC
 CGGCTAATTTTGTATTAGTAGAGACGGGGTTCACCGTGTAGCC
 AGGATGGTCTCGATCTCTGACCTCGTATCCGCCCTCGGCCTCCCA
 AAGTGTGGGATGACAGGCAGTCGAGCCACCGGCCCGCGTGTATCA
 TTTTTGCCTGATGAAATTTCCTGCCACTACTCTGATGGTTGATAC
 ATTTAAATTGTGCTCCAGGGTACAATTATCCTTAAATCTATACCTTT
 TCCTTCTTTATTGACAAATATAATGTTACACTTTCTGTCAATTGCAGC
 CACACCACAGTACACAGATCCAAACAGAGTTGAATATTATTAGTT
 CAGAGTTCAATATTATCACTTCATAACTCATGTCAGGAGTTTA
 TTTGGTACTTCTTACAAAATAATGATGTGCTTCCAAGCATTCTTT
 AATAATTCAATCAATGTTATTAACTGAGTAATACTAGTATCTGTTATT
 CATAAATTCAACAGGAAATGCTTTTACTTATTAGTCCTTGAATTCTGT
 TGTTGTATAAACATCTTCACTGATGGCTTGTGTCTACCAATAGCACTA
 TTGCCAAAAGGCACCTTTCTGTTCTTACTTCACTGGTCCGAAGCC
 TGGTACCAACAACCTACACACAGACTGGAAATGAGCAATTGCCACGT
 GCCCTTAGCTATTAAATGGTGGCACTCCATAACTAGCATCTAACGCTCAAT
 TTCATGAAAGAAATGTGTTCTTATTGTACTTGCAGGCACCTTTAAA
 CTTGTAATCTTTATTCACTTAAATAAAACAGAGTAATAAGAACCC
 ATAGAAGGAAATCAATACCCACGAGTCCACTGATATAAATAATAGTT
 ACATAAATAAATGGGGGAGAAATAACAGCTTCTTACAGAAAAATT
 CAATTAAATAATGAAGAAGGAATTAGGGAAATACAACGTTACCAATTAGC
 AACCACAGTAATAATCATTACAGGCAATATCCAAAATAATTCCAAAGC
 CAGTGGGCAAAAGTTGAGGAGATACAGGATATTAAACATAGTCTCAAAT
 AGCTCATGCTATTATAAATTACAAAAGGAAACATAACAAACTGTATAGTG
 AAGAAACTCAGCAGACACCACCTAGCCAAGTGTCAAGGTTACGTCAC
 TAGTAATAGGGCTTGTGACATACTGGACTCCAATCTGATACACTGATAA
 GGACACATGACTCTGCACTATTCTACAAAAACAGAATTCTAATGTAA
 TTAAGGAAATGTCAGACAAACCTATTCTGAGAAACATTCTATAAAACAA
 CTAACCAATACTTCAAAATTGTCAGGTCTAAAGGACAGGGCATGGTC
 ACAGATTGAGGAGACTAAGGAGATACAACAACTAAATAACACAAATGGAA
 CCATGGCATTCTGATTGGATCTGAAACAGAAAAAGGATATTAGGAAGA
 AAAGCTGATGAAATTCTAATACATTCTGATTTAATTATAGTATTGTA
 CCAATATTAAATTCTAGATTGATCATTACTATGGTTAAGTTTAA
 CATTAGAGGAATCTGGGAGAATGGTATATATGAACTCCACTGTTCA
 ACTTTTCAGTAACATTATTCAAAATAAGTT

>Contig33

GGGAGCGCGGCCACGCTGATCTCTAAAGCTTGTAGACCACATTGGCTCG
 AGCATGGTCATGGCGTTCTG

>Contig34

GACGTCTTACGCTATATTATAAAGAAATATTACCTCCCTGCTGAGCTT
 ACAGGGTGTACCTAATGTCCAACAAATATGAAATCTCTCAATGAATTGCA
 GCACGTCCATATATAACCCACATGGAAGCTGTCTCTTCTCACCTTC
 AACTCCCAGCAAAGAGGGACCTTGTGACTCAAATACATCTTAGCAA
 TATAGAAGATGCTGGAGACTTGTAGGAGAAGTGGAGAGGGTTACAGTGT
 AGCCCCACAGAAAACAACCTATGACCCCATCAGTCATTGTCCTTT
 CCATGCCCTAGTCAGGAAACCACTAGATCCTGGATGGCTTCTTCT
 CCCTCCCTCTTCTCTCTCCCTCCCTGCTCTCTCTGCC
 CATCACCCACTCTTACCTCAACAAAATGACTAGCTCCAGTCTCAT
 CCCTCTTATTGAAAATTTACTCAGGCCCTCTCCCCACTCTGCC
 CAATCTTATTCTTACATCAGACTCACCACAAAGGCCAGGA
 TAATAAACAGGACAAACTCTTCAACACATTAAATGACCATATTGT
 TATTTGGTACAATTGAGGAGTCCAATCCCAGGGAAAGACTAACAAAGA
 AGTCTCTTAACAAAGGTGGCTCCCTACTAAAAACTCTGTAAATGG
 CTGAAAAGAGCATGAGGTTCTGCATATCATTACACATTCAATAGAACG

TCATGCAGCTTTAAAAATGATCTGTAGAGGCTATCTTGTGACAGAAAAG
 GCATTGGAGATATACTGTTAGTGACAAAAATAGGTATAAATGAATT
 CCATGCATGCCCTCATATTTATAAATACACACACATAAAAGACAGGAAGG
 ACAGACATTAAACATTCAAGTCAGGCTTAAGATGATGCATAGTATAATAGTT
 AGGACCATGGCCTTGGGACAGAAAACACTACAGCCTCTCCACCTTATCA
 GCCATGGGACCTTGGGCAATTGCTCAGCCTCAAAGCCCCGTTCCCTTA
 TCTGTGTGCTGGGGTGTGTAAGAGTTAAGTGCATAACACAGAGAGAGA
 GAGAGTACCTAACATGTATTATGTGCTCAGTCATAATGCATCATAGTACT
 CATTGTTACATATGTTCTAACAGTGTCTTATACGTTTTCCCTAACAGTGA
 CCATCTGTTTGGCATTATGAAACATAATGATCCTAACAAATTAAAATT
 AAAAACATAAAGAATATTGCCCAAAAAAAATAAGAACATGAATTCTC
 AAGTAGCCAAGGGCCATAGACAGAAGTAAGCCTTGGTGGGGCTTAGTT
 GAGAGAAGTCTCCAGAAGGTCTTCGTGTAAAGAAGAGGGTAACAGG
 GAGGAGGTGGGGAGAGATGTTAAGTGCACCTCTGCTGGACTCCCTGATTGTTAAGAAGAAT
 GAAAAGAGCAGAACAGTCTCCCTGAGCCCAACTCACTCCCTGACTAAC
 CTAGTCTTGCCTCTCCTCACTCATGGCTACTTCTGTGGTCACCT
 TGTTGAGAAATGGATGTGCAGCCACCTCATCTTTCTACCTCCTTCAC
 ATGTTTAGATAATTAAATGTAGTAGAAGACGGTTACAGCAAAATTAC
 AAAAACAAATATCTCGCTATCTACTGTTGCTATTCTAACCATCCAA
 AACAGTAGCTGAAAACAGCACTCGTGGTCAGCGCGGTGACTCATGCC
 TAATTCCAGATACTCCGGAGGCTGAGGCAAGAGAACACTTGAAACCCGGA
 AGGTGGAGGTTGAGTCAAGATCATGCCACTGCACCTCCAGCCTGGG
 TGACACAGTGGACTCCGCTCATAAAGGGGGGGGGGGGGGGGGGGGGGG
 TATTGTTCAAGATCTGGTTGGGCAAGGGGGGGGGGGGGGGGGGGGGGG
 TCTCGTCTCCGTTCCGAGTGTCAAGGAGTGTAACTGAGACTGGAGGGT
 CACACAGAAGATGGCTCCCTCAAGTGGCCAGCAAAATTGGTGTACAATT
 GACAGGGAGCTGTTGACCAAGGGCCCCAATTCTCTTCTATGGCCCCCT
 CTCGGGCTGCATGGGCTCTTACAGAATGGCAGCTGGATTCCAAGAGCA
 AGTATCACAAACCTACAGAAGAGTGGAGGAATTGAAAGTTCAAGTCTC
 TTAAGACGTTGGCCCAGAAACTGGCAAAAGCTTCACTGCACTGTTCT
 ATTGATCAGTCACAGAACCTGCACCAATTCAAGAGGAGAACATATAGAGG
 ACATCTCTCAATGGGATAAGTGTCAACAAATTGCACTATCACAAATCTG
 TCTTTGGGTACAAACTATTCTATTCTCATTATGCAAAATATACTCA
 CAACCTCCCAGGGGTGCAAAAGCCTCATCCATTATGGCAAAATGTGGCC
 CTTTAATTATATAAAATAATTGCGGGGGCTTCTTATATTAAAC
 TCCCCTG
 >Contig35

GTGCAGAGAAGTGTATTAAAGCCCTTCAGAAAGAACATGCTTATTCGGT
 GAATTGGTAACTTGCTGGGTGCCCCAGGGTTGTGAGCTTCTCCACT
 CAAATTATCAGACCCCTTCATTAGTGGTAGACCATTCCCTCGTCCAG
 GCCAAGGGCACATAGTACAGAGAAATAGGGAGTTGTACCCAGGGAGAGA
 ACTTGGCTCTAACCTGTAATAGAAAGGTCAAGTCTGGTCTGGAGGGTCA
 ATTTGATCTTGGCTCAGATCCAGGAATTGGAACCAAGGCTTGAACA
 TTTTAATGCAGGGGATTAAAAATGATACGAGTCATTCAAGAACATATT
 TGCTTAACATCTAAAGAGATCCCTCAAAACACTAGAAAAATAAGAACAA
 AAATCTAATAAAACAAATTGTTAAACACATTTCACAAATTTTTTTT
 TGGTAAAATTCAAATGTCATAAATAAAGCTAAAGTCTCTTGTGACT
 CGCTCCTCTGCCCTATTCCACTCAAGTAACCACTATTACAGTCTGCC
 AATACCCCTCCAGACCTCTCACCTCTATATACCAATTAGAACACATGGT
 TTTGCATTGAGGATGTGCAGTGTGTTGTTACGTAATGTTACTCT
 GTTCTGTTCCATAATTGCTCTTCTCAATGATTGCTTGGCTATC
 TTTCTATTCACTGAGCATCTCCTTCTTTAACCTACCAATTGTTATT
 AACCTTGCCTCTATCAACAGATATGTAGGGTGTGTTGATTGATT
 AAGTATTATAAAACACGCACTAGTAGATGTCATAAAATTCTTACGGA
 AGATGGCAAGTAGTGGATTGCTGAGCCAAAGAACATGTTAAAAACCC
 AAAAACACTAGACGCTACCAATTCTCTCCAAAATGCCATACCCACTT
 ACCCATAACAGAGATGATTGGAATCTGGCTTCTCACAAAGGTGAGATGCC
 TTACACAGTTCTTCTGCGATGTCTCCCTTGTATCTGAGAGAG
 CTGGCAGAATTGTCAGTAAATCAAGGATAGAGGGTCAAATGACAGCTC

FIG. 4 (13 of 61)

67/118

AAGCTCACAGGCACCTCAGCTTCTCCAGACCACCTGCTTCCTGCCA
 CCAGCTCTGTTCCATCTTATAGAACGGTGCACCTGGGTGTCCTGCCG
 ACAGGCCATGTCATCCTTGCACTGCAAGTATGAAGCAGACAGAGCTAGGA
 GAGGGGCTTGGCAGCCTCTGCCCTAGCTGGAGAACCTCAAAAAGGAG
 GGTATTGAAGTGAACTCCCCAAAAGGGGTGGTCCCCACACCTCAAAA
 AGTGGTGCCTCGAAAGAAATGTAAAATTGGTGTGGGGGGAAAAAGGT
 TATTAGAAATTGGTGGTGTGCGAAAGTATGTGTGGTACGGGG
 AGTACGGAAATTGAGGGTGGGGCGAGGCCGTGTGTCCTTAGCCCG
 GGGTTTCCCGTCGATGTTAAGGGGGGGAGAGGGGGATGTTTCT
 TTCCCGAAGGTTTGAGAACGGCGTGG

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CCCCCCCACCGCCACTACTCAACCAGGCCGTTACGAAACAACTGCCACAT
 CCACATAACCCGCTGGCTACCCACCCACCGCCCTCCCGATCCCCCAATCC
 AAACCTCAACCCCCACCAAGCGCCCTCCCCCTCCCCCACCCCTCAGCT
 CAGCCCCAACCTACCAACCCGACTCGCCCACCGAAAACCAACAGCA
 AACCCAAATGCCCAACAAACCAAGTGTCAAACCCCTCCCATCAGTT
 GGTGGGCCCACCGCCCTCCCTGGCCAGGCTCTCCTTTGTGCGCTT
 GGAGCAGCAGACTGATCTCCAGCCTTCACTCACTCATGTGTAATCTG
 TTGTGTTCATCACTGTCAAGAATCTCTGCATCCCCACTACTCTGCTGA
 AAACACTCTAGTGGTCTCATGCTCATTGCTCATTAAATGAAAGTCTAGATATTAA
 ACGTAGAAGGCCAGCAAATTGCCCCATGCCACCTACCTCTCTAAATC
 TTTCTCCTTACTCTGACAGACTCTCGCTGTCAATTATGTATTCTTTT
 ATTGCTCTTCAAGTATGAAATAAGAATTTTATTATTATTATTATTATT
 ATTTGAGACTGGGTCTCACTCTGTTGCCAGGCCAGAAATGCAATGGCA
 GTCATATCTCACTGTAACCTCGAATTCCCTAGGCTCAAGCCATCCTCTGC
 CTCAGCCTCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGC
 TAATGGAATAAAATTACAATGCCAATCTTAATTTCAAAATTTAAA
 TTACATTGTAACCTAATGCCCATGCAATTACTTTTCACTGGGTCAATAG
 CCCTCACTTGGCAAAGGTCCAGGCCAGGTAAGGCCCTACTTTTCC
 AAACTCATCTTTGAAAGACATAAGTGCCTGTAAGTTGTACCACTAGG
 TTCTAGGAATTTCATCAAAGACTTATCAGACTATTCTCTAAGTT
 GAGAAAGAGCTGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCA
 CTGAAATCAGGCCAGAGGTGCTGGAAAGAGCAATGAGGAACACCAGCAG
 CAATGAGGAGCCGGTGTGATGATTTGGCTTACAGGGAGGTGTGACCA
 CCGATTTATCTCTACGTGGATGAACCACAGCTGTCGGCTCCCTGTCTC
 CAGGACATCACACTCTCCACATTCCCTCCCATCTCCGGCTCTGCTTCC
 CGGGCCCTCATCTGCCCATCTGGGTGAAACACTGGTGGTCAACTGCT
 GGGCGTACCTCCCGCTCTGCACACCCCTCCCTGGCCACCCACCTCT
 CACGGCTCGACTGCAGAGGCCGATCTCTAGCTCCAGGCCATCTGCC
 TCTCTGAGCTCTAACTCATGTAAGCGACTCCTGCCGGTGTGCTC
 AGGCCATCATCTCAAAGCATTTCCCTCAGAACACCATGCTCTGGC
 TGCTCCCTCCAGAAGATACATCTCTCAAGCACATCCCCGGCTCTCACC
 TGGATGACTGCATTCACCTCTCCACATTGCCCTCCCTGGATGTA
 TATAGATTGTTAAATAACAAATCTGATGTGCTTGTCTCTGCTTGAA
 ACACCTCAAACACTGCCCTCAGGATAAACCACTGCCCTGACATGTTACA
 GGTTGCCCATGGCCTGCCCTGCCATCTCTCAGCCTCATCTCATGCC
 CTTGCCCTCGCTCTGGCTTCTGCCTCCCTAGCCCTCCTTAGGTT
 TCTAACACACCATAGTCTCTAGTGTGGGCCCTGCAAGTGCTGTT
 CCATTGCCTGAGACATGAATCCCTCCCTATCTCTACCTGCACCTCAT
 CTGATTAATCCCTACCCCTCTACTCATGATGTTGCTTCTCAGGGACTC
 TCTCTGACTTTAAACTAATCAGGGTCTCCCAGTATAATCTTCA
 CACTCTGTATTACTCCTTCTTAATGACCACCTGCTGTAGACAGAAATGTT
 TGTCTCCTCCAAAATCATATGTAACCTCCACCAAGAGCGATGATTAG
 AGAAGCCTCCC

>Contig37

GACTGACATTGAGAAGATATTAATAAGAGCACTAATGATGGGATTGCA
 CCATGCTTACTGACTCCAGAAGCTTACAGTAAACATGAAATCAC
 ATAATTCTCCACTTCTACTGTGTTCTGCTGGGCTCTGCTCTGCT
 TACTGTCTAATATCTGGCCCTTAAAGTTGCTAATCTCCAAACCTCA

TTCCCTGTGACTGGGCCGTTGGTCCTTGATGGGCCTTGAAGATACT
 CTGTACACTTATCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCT
 CATTGCGCTCCTCCCTCCACCTAATGGGATTTGCTCATACCCGTGTG
 GGACCCCTCCCATTTCACCTGAATACTTATCAAGACAACGCATTGC
 CATACTCCCTCGTACCCGTCTGGGCATCAGACTGAATGTTGTTCCA
 TTGAGGATCTGCAGCTGCATCAGTTCCCCAGCACCGTCAACCCCTTGA
 GCATGGCTAGTCTAAAGCAGAGAATTAGCCTTCTATCCCTGCTGCTAT
 ACATGCTGGGACAAATAATAAGAAATGACAGCATTATGATAATGCAGG
 CTGCAGGAGGCAGGAGGGCAGGAATCAAATTCTGTGCTTATCAAATAGTGC
 CCAATTCTTGAATATTGGACTATAGAATATGTCATGGATCTATGCTCAG
 GTGGGTTCCCTATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTG
 TCCAAGAGGGAGTTCACTGTCACAGCATAGGGTCAATTCTGAGAATTACT
 GGCCCACACTTGTGTGGAGACCTCCAGAGAACAGAACAGAACATCTGGGTTGGTGC
 ATGTAATTCCAGGAGGAGAACAGTGGCAGGATGCCAGCCCCACAATCAG
 AGGGGAAGGGCAGAGCCACATGTATGAAGATCCTCTCCCAGTACGTGC
 CAATCACAGGGCTTCCTAGCTTTGGCCAAGGAAACAATGTGGGAAGCA
 AAAAAGGACAATTTCCTCCCTTGCATGAAGACTGAGCAGTTTAC
 AGATTCCCAGGGAAACACCCCTCCACTCTGGGTTGAATGTGAGTGAGA
 CATTCACTGGAACACTAGAAAAACTATTCTGAGGCCACTCACCTTAC
 CCCTAGAAAGTGTGGATTGTCTTCATCTTGCCACAGTAGAGACTGC
 TGATGACATCAGAACATTGGCTCTGGATTAGACAGATATGGGTACAAAT
 CTGAGCTCTCACTTATTAGTGTGGGATGTAGAGCAACTTTAAAATCC
 TTCCAAACCTCAGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCC
 ACCTAAATTGGGTTTTGAGAATTAAAAAGTTATTCAATGAACAGCATT
 TAGCAAGATGCCATTGAGAAAATAACAAATTGTTTATTATTATTG
 TTATTATTAAACATCTTCTGCACCTTCTGACTGGGGCATCGTATCAT
 CAGAAAATACTTAGGATGGGATGGATTCTGCATGGCTGAGTCAGGGT
 CAATAATGGAGGAGTGAAGAACAGGAAGAACATGGAGGCAGAAATCCCAGGA
 GCCCAGCATGGTACAAGGCTGAGCTAGTGTGAGAGCCTCTGGAAACA
 GCCACAGAGCTGCATCTGGCCCTGGAGGAACCTCTAGCTGGCAGGA
 CCAGCCACAAACAGTGGCAGGGATTCCCAGGGCTGGCTCCTCAGGA
 GTTCAATTGGACCAAGGCTGCTGGAGAGGGTTATAACAGGGATCCTC
 CCTACTGGCAGGTGATTACCCCTCGGTGAGAAGCTCAGGCATTGTTG
 ATGGAAGGTGGAAGGCCCTGTGCTGGGCCAGTGACTATCAGGGATGGGCG
 GGTGGCTGGAAAATAGCAAATAAGACAATATGATAAACACAGTTAACACC
 AACTATGTGAAGCTACAATATGGGTATCTGTAATAGACAATTCAATGT
 AGAGAATAATTAAAGGTGTCATTCTCCCCCCAATGCCATAAGCACACCG
 GCCTCTGCCTGGTTCTCACTGTGGAATGTCCTCTGGTCTCCTCATGC
 CCAGAGAGTGGGAAGTACTCCTACTTTAACACCGGCTTCTGTCAATT
 CNTGCAGCCCTCCTCAGCCCCCTGACACAGGGAGGTTCTCCCTGCTG
 CTGAGTGCTTGTACTTGTAGTGGTACCTGCACACAGGTATGGTGTG
 CTTGTCTCACCCCTACATCACTGTAAGCTCCCAGGGAGCAGGCTTCC
 GTTGTACTCACCTGTGATCCTCACCTCCACCTGTAGTGCCTCAAGCA
 TTCTGTAGAGCACATGGACGCC

>Contig 38

GACTAATAAGTACTTCATTATTGGTATTTCAGAACACATATTGT
 AGGAAACCATCTTCTAAAAAAAGTGTCTTTAAAAAGGTGAATA
 ATTGTTGTCTAATTCAAAGTTATTGAAAGTTATGTATAAAACAAGGT
 AAAGGAACAAGGAATAAGGGAAATGTAAGAAAATTATAGAAATAAGT
 GGTATTTGGTAAGAAAGCTAAAGAGAAATAATTAGGTAGAAAG
 AATCTTACCTAAATTGTGCTAGAATAAGTGACTGGCTAAGAAAGGG
 ATGTTCAAAGCTATTATGACAAACCCACAGCCAATATCATACTGAATGG
 GCAAAAGCTGGAAACATCCCTTGAGAACTGGCACAAGACAAGGATGTC
 CTCTCTCACCCTCTATTCAACATAGTATCGGAAGTCTGGCCAGGGCA
 ATCAAGCAAGAGAAAGAAATAAGGGTATTCAGAACAGGAGGAAAGT
 CAAATTCTCCGTTGCAGATGCATGATGCAATTAGAAAACCCAT
 CATTCAAGCCCCAAAACCTTAAAGCTGATAAGCAACTTCAGCAAAGTCT
 CAGGATAACAAATCAATGTGCAAAATCACAGGCATTCTATACACCAAT
 AATAGACTAACAGAGAGCCAATCATGAGTGAACCTCCATTACAATTGC
 TACAAAGAGAATAAAACCTGGGAATACAACATTACAATGGACATGAAAG

FIG. 4 (15 of 61)

69/119

ACCTTTTCAGGGTGAAC GCAAACCAC CTCAGGAAATAAGAGAGGA
 ACAAAACAATGGAAAAACATTCCATGTTATGGATAGGAAGAACATAT
 CGTAAAATGCCATACTGCCAAGTAATTATAGATTCAATGCTATCCC
 CATCAAGCTACCATTGACTTTCTCACAGAATTAGAAAAACTAATAGCC
 AAGACAATCCTAAGCAAAAGAACAAAGCTGGAGGCATTGCTACCTGA
 CTTCAAACATACTACAAGGCTGCAGTAACCAAAACAGCATGGTACTGGT
 ACCAAAACAGATAATAGACCAAAAGAACAGAACAGAGGCCTCAGATATA
 ACACACACATCTACAACCATCTGATCTTGACAAACCTAACAAAAATAA
 GCAATGGGAAAATAATTCCCTATTTAATAAATGATGTTGGGAAACTGG
 TTAGCCATATGCTGAAAACGTGAAACTGGACCCCTCTTACAACCTTAC
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 GAGTTAAGTATTAGGAGGATTAAATATGTTAAAGTTGTTAAAGTTGAAAAATCA
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 GCCATGAAGAAAGAGTTCTCACACTTGTATCCCTGATCATGAAAAGACT
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 CCATTCTCAAGTCAGAAGGCCAGTGCAGAGAGAGCTGCCAGGTGGCTTC
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 TAAGTATGCTCTTTAAAATATATTATTGTTAATAAATTGAGACAGG
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 CATATACGGCTCTTAATGC

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CGCATTAGCCCAAGTTTCTCAGTGTAAAGGTTTGTACTCTGTGC
 CCAAATGCTCTCCAAAAGGTTAAGTTTACCTTCTGCCAACATT
 ATATGAAAGTGTCCACTTTGTAGACTTTACCAATGCTGACTACTTTG
 GTTCAAAAAAGCTCTCAGTAATTCTATTAAATTACTTTACCCCTTT
 TATTGAGGGTGTCAACTTTTATTGTTAGCATATTCTCTCTGGGCTCCA
 TTGGACGCCCTGGCAGCTTTGGTAGTAGGTGCCTTAGAAAAGTCCT
 CTCGTCTGGCCCTTCTGAGCAAATCTAGTGAACAGAATTGGCTCATGC
 TCAGCATTGCTTAATACGGTTGATCCAGGGCTAGGACTCATCCTTCAT
 TACCATCCACTTGCTTAAAGCAAGGCTCTATTAAATTAAATTG

CATTTCTGTCCCAGCTC1:TAGTTCAATTAAACAAAGGCTT~~AGAAAAAC~~
 TCCCAGTAGATGCCATGGTCCTCTTTAAAAAATTGGAGCTGTT
 CCCTAGCCTAACCTTCTCAGGGCAGGAGTTAAGTCCCTCTACTGCA
 TTCTGTGAAGATGGTGATTCAAGAGGCAGGGCACCTGTTGCTTGTGAA
 ACAGTCCACTCTGCAGCTGGCAGCTCTGTTACTAGAATGTTCTCCCTC
 TGGGAGCCAATATTTGATGTCCTCTGTGAATCTCATGCTTATCCCA
 TCGTTTATGTCTTGAAGATGCACAGGCTGACACCACGAGGTAGCCCT
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 CCTCCAGAGCTGTTCTTAAGCCCTTGTGGAGCTGATTGCTTCC
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 TCCCAGTGAACATCATTTCCTCTAAATCCTAGCAATTGTC
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 GATTGAGGAGATGACAGTAGTCCTCATCTGAGGAGGGCGTGTCCA
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 ATTGTCATTGCAAAAACAGAGACAATTCAACGTTGTCAGAGTGAATG

GATGAGCAAGCTGTGGT GTCTATGCA...GGTATCCTACTCAGGCCAG
 AAAGATATGGCTAAT
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 GACAACAATGTCATGCATAAGATGACGATGGCCTGGGTGATTGATGCAA
 CAAGGATAAAGAAAATAATCAATTGTCCCCATTTCAAAGACAGATAG
 CAGCAGCAAGAGTGTAAAGTCTGAGGAAGTCATATTCCCTCCCTACAA
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 TTCAAAACTGAGGAGGATCATTAAATTAAATGTTACCGCTGCATGAAA
 TCTCCCTGGGTCTGCCCTCCCTCCCCACCCCTCCACTTGGGCCGGG
 GCACAGCAGTGATTCTCACCTCTCAGAGTGAGCCAGTGTGGCTGCAT
 TGAAGGCTCCAGATA TGCAAACAGGGCAGATATTCTGGACCAGGGTGCA
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 CTCTGGTATGGGTGGGACAGAAAAAAGGATTCAAGGGCCAAAAGGGT
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 GGGCGAGTTCATCCACAGCCACCTGCAGTGTAGCACCTAACGCTGAGT
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 TTGCTCCCGTAAGTCAGGGCTCATTGTGGCTCTGCAGGCTTGACTTCA
 GGGTTAACAGAGAAAATGAAGGTACAAGTGCCTGTGAACCTGAAACTC
 CAAACCAGTCATTCTCAAAGTGCCTCCACCAGTCTAGCACATCAGCATC
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 TGAATTAGAAACTCTGGGAATGGGGCCCTGCAATCTATTCAACAGGTCC
 TCCAGGTGATTCTGATGCAAGTTAACGCTGAGAAAACCTGTCATCTGCTT
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 ACCCGAATCCCTGAGAATGGAGCTTCAGGACTGCTATTCTCAAAGTTG
 CCTGGTGATCCTGAGATGGGTTGGGGACAGAGATCCAAGGTGCTACC
 AGGTGAGGAATTGTTAGAAGGCAAACCTGGCTGTATCTAGGGTGCTT
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 CTAGAATGGGATTGCTGTCATGGCATGCCCTGGGTGACTCTGATGT
 ATAGCCTGGCTGGGAACCACCAAGAGGATTATCTCCATTGACCAAGCTG
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 TGGCCATAGGTGTGCAGGGCTGCCATGTATTAAAGCTACAGATT
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 CTCAAAAGAACATGAAACCGTGTCCAAGTAATTAAACTGTGCCCAGAAAA
 ATTCAAGAACATTAAATAATTAATGATCAAACCCAGCAAGG
 TAAATTCAAATGTCGGCATCCATTAAAAATTACAGCCTTGAAAAT

FIG. 4 (19 of 61)

73/118

TGGCGGGAAAATATTA: CATAATGAA. GAAAAAGCAATCAAGAGA/
 AGGCCTAGAAAGTATAACATATGATAAAAATTAGCAGACATTAATGGTTAT
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 TCACCAGTCAGTGGGAAAACCTCATATTCTATGGAGCATGGTAGAGTA
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 CTCTGGGAGGCCAAGGTGGTGGCTCACCCGGAGGTCAAGGAGTCAAGAC
 CAGCTGGTCAACATGGTGAGACCTCATCTACTAAAAATATAAAAATT
 AGCCCAGCATGGTGGTGGCGCTGTAATCCCAGCTACTCAGGAGGTTGA
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PCT

AGCAAAGAGAACTGACCCACATTAACGTAGAAGTCTTACTTTA¹¹
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 TAATTTTTCTGACTTTGAAATACTGAGAAGAGCTCATGACTCTCCC
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 TTTAAGTGTCA¹¹GATTCTCCCAGCTGACTTTTCTTGGCTTAGTGAT
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 CAGGCC¹¹TGAGCTTCTGATGTGGAGGAAAGAGAAAGAGAGAAACT
 CCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGGACGCGAGAA
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 TCTCTGACA¹¹ACTGGC¹¹AAAGACCCACAGAAA¹¹ACTATCTCTAGACCC¹¹TAC

CTGTGGGAGGGAAAGI...TTTCAGATCA...CTACAGGAAGCCACCTGGAA
 CTCAAATGGCTTACAGTCTTCATCCAGAGGGCTTCATCTAGTACATA
 CCAGGGCTAAGCCTGGGTGCTGGAGACATGACGGGGAAACCCATTACCA
 TGGCTTTGTTACTGTGACATTACACATCTAGGGAAAGCAGCAAAGGGAG
 GGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAAGGGCAAGGGAGA
 AGCCAGCCTGTCTGAGCACACACAGTGGTCCATCTAACTGGGCTCAG
 TGCCAGGTTGGACTGGAGATGGGGCTGAGGAGCTGTACAGAGCATTCTG
 GACACAGATGTACATAGTCCCTGAGGTTAGGGCTCTAGGCATGGCAG
 CATTGCTTGAGTTTCTCTTGTAAATGTTGCCATTACATGACAATGTGG
 AAGATGGGTCTTGCAGAGAAGGGCAGGGCTGTGAGACCAGTAGGAGAC
 TAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGGGCAAGGTG
 CAGGGCCCAGAGAGAACAGATGGCTCCTGAGGTTTAAGTAGGTAGAA
 TCAAGGCAGCTGGTAAAGATCTTTATTACATATAAAACTGGAATAAGCCA
 TCTGCTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGACAGAAATGG
 AATTAGAACAAACCTGGAGGAATGGAATTAGAGTAGAGAGTCCAACA
 CTGGCTGCAATCATAAAAATGTAACAAACAAAATTGCTAGGTGTGC
 TTACTTAGAAAATTAGCTGTCAATTAGTTCACTGTGTTATGGCTT
 AAATGTGCCCCAAAATGTGATGTGTTGAAACTTGATCCCCATGCAA
 CAGAGTTGAGAGATGGGACCTTAAAAGGTGATTAGGTCTAAGGGTTCT
 GCCCTCATAAATGAATTAACTGTTATCATGAGAGTAGATTCTGATAA
 AAGGATGATCTCTGCCCTCTCCCCACAGCCCTTGTGCTGATGCTTCTG
 CCTTCCACCTCTGCTATGGGATGACACAGCAAGAAGGCCCTACCAGA
 TGCAGCTCCTGATCTGGACTTCCAGCCTCCAGAACGTGAAAGCCAAAC
 AAATTCTGTTATTATAAATTACCCAGTCTCAGGTATTCTGTTAGAA
 GCACAAAATGGACTAAGATCATTAGATTATCATTGTTATCAGACTGTTG
 AAGTAAAAATAAAATCAAATAAAGAAAATTAGAGAGCTGCATGCAGCA
 GCTCATGCCTATAATCCAGCACTTGGGAGGCCAAGGCAGGTGGATTGC
 CTGAGCTCAGGAGTTTCAGACCAGCCTGGCAACACGGTGAACCCCTGTT
 TCTACTAAAATACAAAAACTAGGCCGGCGCGGTGGCTACGTCTGTA
 TCCCAGCACTTGGGAGGCCAGGGCGGTGGATCATGAGGTCAAGGAGATC
 GAGACCATCTGGCTAACAGGTGAAACCCCGTCTACTAAAATCAA
 AAAAATTAGCCGGCGCGGTGGCGGGCGCTGTAGTCCCAGCTACTCGG
 GAGGCTGAGGAGAACATGGCGTGAACCCGGGAAGCGGAGCTGCAGT
 GAGCCGAGATTGCGCCACTGCAGTCCCGAGTCCCCTGGCGACAGAGC
 GAGACTCCGCTCAAAAAAAAAAAACTAGCCAGGCATGGTGGTGT
 GTGCCTATAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATTGCTTGA
 ACCCAGGAGGTGGAGGTTGCAGTGAGCTGAGATCATACCACTGCACTCCA
 ATCCAGCCTGGGTGACAAAGCAAGACTACATTCAAAAAAAAAAGAAAG
 AAAAAGAAAAAAAGAAAAAGAAAATTAGAGAAAGGGCAGGTATTAA
 CCCAAATATCCCACCATAGGGACACATTAAAGTTGCTTGGCCACTCCC
 CTAGCATAATATATGGAATGTCTCAAGGACCCCTCTGTTGTAATACAAG
 GCCCTGCTGGACTTAATACAACCTGCAGGCTTGTGAGATCCCTACTCTGTT
 GCCATCTCTCATAGGATTGAGACCAATCCAAATACTTAAAGAGCAA
 CACTCACAAACATGCAAATCAGAGCAGAAAAGAAACTCTAAAAGGCCCT
 GAAACTACACTTATGAGAGAACAGAACATAGGGACCTGAGGGTGGTAGAAT
 TTTCTCTCATGCATCTATGTTCCAGGGCTCACTTCTCAATAAAACTCT
 TAAATTGCTTTAAAGTAAGGGACAAGCAAACATTACATTAAAGAGAAA
 TCAATTCTAAAGAAGGGGGATGTCCAGGGTACTTTGCTTCCATGTTT
 TGCTTCCATGAATTGTTAACAGAAGATGAGAACACACAATTAA
 TTGCAAATCAAGGAAATCCACTCTAAACATCCCTGGTTCCAGGCCA
 GTGTCACAACACTGAAACACATATTGTGCTTAATTATGTGTCAAAATTAG
 AATGACAAGGCAAGAAAAAAACTCTCTGATTAAACTAATAGCAGCCAA
 CACAGACAGCTGTGAGCTGACTCTGCTGGTTATAAAAGGCAGAAGA
 AGCAAACGGCTCTGTGACCGCAACAGGAAGGGCTCTGCTCTAATAAA
 TAAATAACATTAAATTATTCTCCCCATTGCAAAGCATTCTCAACTC
 ATTATCTCATCTGACCAGGTATTATTGTATCTGACCAAGAACTGTATAC
 NAAATAAAAGAATAAAAATAAATATGGGCCANGCACAGTGGCTCATGCTT
 GTAATCCCACACTTGGGAGGCCAGGGGGATGACTTGTAGGTAG
 TAGTTGAGACCAGTCTGGCGACATGGCAGAACCCGTCTACTAAA
 ATACAAAAATTAGCCCCGATGGTGGCACATGCCGTGTAATCCCAACTACT

TGGGAGGCTGAGGCACGAGAATTGCTGAACCTCGAGAGGGGAGGTGCA
GTGAGCCGAGACTGCGGCCATTGCCCTCAGCCTGGCGATGAGAGCGAA
ACTTCATCGAAAAAACAAAACAAAACAAAACACCTTAGAAGA
AGCGTTCTCCTCTGCTTCTGAAGACACTCTACGCTGAAACAGTAAC
TTCAATAAACCATCTCTCACCAGCACTCTGCGACTTGCCCTGAAATTCC
TTTGTGTGCAAGATCCAATAAGCCTCTCTGCGGTCTGGATGAGAACCCCT
TTTTTGGAAATACTCTGACACAACAAATTGCAAGAAAGAAAGTCTCACATG
TATAAAATAAGCAAAAGATTCTCTGGCATCTGAAGAAACAATTCCCTG
TCAATATTAGTATCACTATAAGTGTAGAACAAACCTGTTGTATGATGCTAC
ATAAAAGTATATGAATCTGAATACTGTTGGATACAAGGGAGACTATNNAA
TGTAAATACGTGCCCGAAATGACTACACTGTTGGTATCTTCTTCAAG
AAGCANAATATTGCTCTNAACATCCTGTACATGGTATAAAATTITA

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CCCAGCAAGAACACCAATAACGGGGGGGCGTTCTTGTGAGGGGTGG
GGAGGTCAATTTCGGAACCTGCAGCAGTAACACACAAAATTCACA
GCTGCTACCAGCTTCCAGGAGAGGCCGTGTACCTGGAGAGGAAGCA
AGTGCTCCGAACCTGACTGATGTCCTAGATTCTGCAATCGTAGTC
TAGGGACAGGCTGTAGCTTATCCTATAGGCTGGCTGGAGTCAGCAAGC
ATCTGGCTGGCAGAAGATAAAAGATGCAAAGGTGGAGGAAGCATACGT
GGTCTGGAAGACAGACTGTTGGGTGGCTGTACACACCCCTAGTT
AGAGGTAGAGGGTAAAGTCAGTGTCTCTGCACAGGCCCTTCCCCAC
CTCATTCTCATTCCTACAGCCTGCTGAGTTATTCAAACATCTG
ATTCAACTGGAAGCTGGGTGAGGATGACCTAAAGGACTAGTGTGATGCC
TGCCCAGGGTGTGGGCCATAGTCAGACTCAGAGCCTCTCAGCCT
TTAGCACATCTCACCCACATCTGGTCCTAATTAGCAATATGAAAGCA
AGCCAAGTGACAAGATTGCTCTGGAAAGTCCAGAAGCACTCCTTTC
TCATTTGTATAAGCATAATGATTGCTTACATAAAATCATGAAAATT
AAATCCCTCTCAGAAATCAGGTCAAAACATGAAATGAGCAGCATGTGGG
CAAGAAATCACAGGGAAAGGTAGGTCTGGAAAAGAAGATGGCAGGGAG
GAAGAAAGCAGGGTGCAGGGGCCCTGGCTGTCCAAGTCAGGTGGC
TCACCGCTCTGAGAACATTCACTTCTGGTAAATGGGCAGTTGGAGA
TAGAAGGGTGGGTGAATGCCAAGACTGAGCACAGCTGAGGTCACTGCTG
TGCCTGCAGTCAGGGGGAGTAGAAATCCTGGGCCATCTACCTCCGA
CCTCATTCTCTCTGTAATAATGTTGGGGTGGGGAAAGTCTGGTCA
TCAGCCCTAGCATTCATGGTTCATTCTCATCAGTGTGAGGAAATCAC
CAAGCAAGAGAACAGGATGGAGAATAACCGGATGGGTGCAATGGAGGTG
CTATTTCAGGTGAGGTGGCCAGGGAAAGGCCCTGTGAAAGGGTGGCTTGA
CAGGTGGCTGAATGTACAGAACGCTGCAATCATGAAAGATCTGGGTACA
GCATGCCAAGCAGAGGAAATGCGAGTGCAAAGGCCCGAGATTGGATGTG
GGCTTAGCACAAATGTGGCATGGCAAGAAGGCCAGTGTGGCTGAAGCAGC
ATGAACAATGGGTGGAGGGCTGAGAGGACAGAGGAGCAGGAAAGAGCA
GGCTGGTAGGAGAGGTGTCACCTGATATATGATGCAAAGCCCTTGA
GGTCCCAAACACAAAAGCAATGATCTAATATATGGTTAAAAATGCCA
CTCTGGCCGGGCGCGTGGCTACGCCCTGTAATCCAGCACTTGGAG
GCCGAGGCGGGTGGATCATGAGGTCAAGGAGATCGAGACCATCTGGCTAA
CAAGGTGAAACCCGCTCTACTAAAAATACAAAAATTAGCCGGCGCG
GTGGCGGGCGCTGTAGTCCCAGCTACTCGGGAGGCTGAGGAGGAGAAT
GGCGTGAACCCGGAGGCGAGCTTGCAGTGAGCCGAGATTGCGCAGTG
CAGTCCGCAGTCGGCCTGGCGACAGAGCAGACTCCGTCTAAAAAAAA
AAAAAAAAAAATGCCACTTTGCTGTAAAAATTGACCTGGGGAA
AGGAGGAGTAGAAATGTCAAAGTGAAGCAGACACTCAGGAGGTCA
GCAATGGACTGTGCAAGGAGAGACTGACATCTAGACTCGGGCAATAGGAG
AGAAGGTGGTAGGGATTATCTGGGATAAAGGCAACAGAACTAGCTG
ATGGCGTCAACGTAGGAGATGAGGGAAAGAAAATCAAAGGGCATTCA
TAGGTTTGAGGGTTGAGTAACCTGGGATATTAAAGAAATGGAGAAGTC
TGGGGAGGGGCAAGTATTGTGGGGCAGGGGTCAAAGTTCTGTATTTT
GGCCAAGTTAATTAAATTGAGATACTCTTAGGTGTCAGTGAAGAGAT
GTCAAACAGTCATTGAATACAAAATCTGAATCTAGCCAGGATGGTCT
CACACCTGTAATCCAGCACTTGGGAGGCTGAGGTGAGGAGGATCACTTG
AGGCCAGGAGTTGTGATCAGCCTGGCAATAGAGCAAGACCCCTGCTCC

FIG. 4 (23 of 61)

77 / 118

ACACACACACACACACA.. AAAAAGTCA₁ CAGGCATGGTGGCAGATGC...
 GTAGTCCCAGCTACTCAGGAAGCTGAGGAGGAGTACATTGAGGCCAT
 GGTTCAAGGCTGCAGTGAGCTATAATCACATCAACTACACTCCA
 GCCTGGATGACAGAGAGAGACCTCATTATTAAAATAAAATTAAAAAA
 TTAATTAAAATAAATCCAAATCTTCCTGAGATTATTCAGGAGTAA
 CTGTATGTAGAAGGCATAATGCCATGGGTACATGATACCATCTAAT
 GAATGCCACTGGAAAAGAGAGAATAGCTAAAAGTGCAGCACTGGGCACAC
 CAGCACAGTGGAGGTTGGAAGGAAGAAATGGAGCTAACAAAGGAGACAAAA
 GAGGAGTAGCCAGTGAGAAGAGAGAACATCTGGAGAGAAGAGAGAGCAG
 CAAAAGGTGGGTGAAGGAGAATGTGGTCCACCAGGCCAACAAATGCTGAG
 CAGTTGAGTAAGTGAGGACCTGGCACTGAATTGGCAAGAAAGAGGATG
 TCAGCGGCCCTAGAACAAAAGTGAAGAAGAGCTTGAGGACGGAAGCCTGA
 CAGGAGTGAACTGAGGAGAGAATGAAAGGTGGAGACATGGAGCCAAGGAG
 CACTGAGACTCCTTGAGTAGTTTGTGAAAATAAAAGTGAGTCAGA
 GACGGGGCAGGGGGACAGAGAAATGCAGGGTAGCTGGAGGGAGCCACAG
 AATCAAAGAGGGTTTTGTGTTAACATGGTAGTTGTCACATAGCACAT
 TAGTAAGTTATGTGAATCACACAGTAGGTGAGACAGATCACTAATGCAG
 GAGTCAAATCCTTGAGAGCCCCAGAGGAGGTGATGAAGGGAGTGATG
 GACATCATTAGTCAGATGCAAGTAGGTTAGCAATTCTGGGTACAAATAGGA
 GGTGACTCCTTCTGATTGCTCTGTTCTGAATGAGATAGCACATAAA
 GTCCACTGCCATGTTAGCTGTTGAAGTCCTGTGGCTGTCACTGCTGT
 ACAGACTGGGCTCTCTCCAGCATTCTCTCAGACTAACGCTGAGCTG
 CACTAGCCGCTGCCACATCCTCTGGGGCCATCCTCTGCCACACTCCACA
 TATTGCTGTGGTTGCTTGCAACCCCTGGAAGGCTACTGGCTGCTCT
 AGAAGAGTCTGGCGGCATCTCTCCCTACTCGTTATCACATGGTGT
 AAGCAGTGGCCACACACTTAGCTGGGGATGGGCATCACAGGAGTA
 AATGCGAAAGACTGCTCAGATTTAAAGCACCCTGAATCAGTAGAAATGA
 GTTTAGAATTGAGTCAACACACATTAAAAAAAAAAACAGGCAC
 TAAAAAAATTAGTTGAGTAGGATAAAGCCATAAAAGATAATTAACTACAAC
 CCAGATAGGAGGTGCAAAATTGCTCTACATAATCAGATGGAAAAGTT
 GAAAGCAGATAAGATAAAATAGGTAAAGCATGACATTAAAGGTATTCA
 GGGACGTGGTTACAAACCAACTACAACCTAAAAGTCTTAGGACCTCTC
 GCTGACTTAGGAGCCTGATCCCAACTTGGAGAATGACTCAGTGTGTTACC
 CTGTGGCTAGTGTAGACCAATGATCCTGTCAGAGTCACAGGCCAACAG
 CCCATATCAAGTAATTGAAACTTGAECTCAGAACCTCAGTGTCAAGAAC
 TTTGACTTAGGAACCACCTGTAGTGGTTAAGTGCACATTGCAACCCCTAG
 TTCAGGGCTTACAACACCGGGGGGGGGAGGGGAGGGCATAGAGCTGA
 TGACCTAAAGGAAACCCATTGCAACGCTTTGTGTTAACGTTACAAA
 TAAGTGTGTTAGAATCCTCCAGGTATGCCTTGTATTAAATGTGT
 CTGAGACAATTCTGCACATTAAAGAATATAAAATTACCTTGTAAATTCC
 AATTGAAATGTGTAATTGACATTAGACTCTATTAAATTGAAATGTC
 TAAAACAATGTGGTTAAGTTGAAAGGTGTGAAATTGAGTCTGAT
 TTACTACATTTTTTAATTCTTTGGAGTTAGGGATTGC
 TTAGATGGCTAGAAAGATCGCTAGGCACATGTCC

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GATGTGTGTACGTGTGCAAATACCGTCCTTTTGTGTTCTTTGTT
 GAAACAGAGTCTCACTCTGCGCCAGGCTAGAATGTAGTGGCGTGTGATGT
 CAGCTCACTGCAACCTCCGCCTCCAGGTTCCAGTGAATTCTCCGCCTCA
 GCCTCCCAAGTAACGGGATTACAGGCGCCACCAACACGCCAGCTAAT
 TTTGTATTAGTAGAGACGGGGTTTCAACATGTTGGCCAGGCTGGTC
 TCTAACTCTGACCTCGAGATCCACCCACCTGACCTCCAAAGTGTG
 GATTACAGGCATGCCACCATGCCAATACTGTGCCATTATTAA
 TCAGGGACTTGAGCATCCATGGATTGGCATCCATAGGGTCTGTAAAC
 CAATACTGCACAAATACCAAGGGACAATGTATTCTAAAAGACCAAAAA
 TTAATAAGCAGGACGCTGAAGGTAAATTGCCCAATAAGTCATGATCCCT
 TGCCCAGTGTCTGAACCTCAGCCAGTTCTACTCAGGACCTATTGGCT
 GCAGAGGTGGTAGGAACCATAATGAGAATCTGCAATATCATGGCAAGTAT
 GCACCTTAATGATATCTGCAGTCCTCCCCAAAAGGACCTTACATTAC
 ATACTGCTATGTCTGCGTGAAGGGTAATACTCAGATTTTTTTT
 TTTTTTACACAACGTCTACTGTGTTGCCACACTGGAGTGCACGGCT

FIG. 4 (24 of 61)

78/118

CGATCTTAGCTCACTGC . CTTCTGTT1 . TGGGCTCAAGTGATTGTC
 GCCTCAGTTCCCTGAGTAGCTGGATTACAGGCCCGCCACCATGCCCTG
 GCTAATTTGTATTTAGTAGAGACGGAGTTTGCCATGTTGCCAGG
 CTGGTCTTGAACCTCTGACCTCATGTGATCCGCTGGCTCCAAAGTGCT
 GAGATTCAGCGTGCAGGCCATACCCGGCCGGAAATTCTTATATATTC
 TGAAAACATAATCCTTGTGAGACATAAGTGTGTAAATTATGTATCCCAG
 TTTGTGGCATGTATTTAATTTAATGGTGTCTCAATGAAAAAGC
 TTAAACACTAAATGAGGTCAAATTGATCACCTTTTATTATGGTTGATT
 CCTTTGGTGTATGTGTAAGGAATGTTGTTCCCTGTCCTGCCAAAGTTGC
 AAAGATTTCTTGTGTATTTGCTTAAAGTTAAAGTTGCTTTCC
 CATCTGTGCACATTCACATTGCTACATCTCACTGACTGCTCCTCTGC
 TGCAGAGCAAGCTCCATGAGAGCAGGAGGATGGTCCCTGCTCTGTTG
 GTCCCCAGAGCCTATGTCATGACTAGGACCTGGCAGGGGACTAGTGAGT
 AGCTCCTGACTAACTGACTCAATGAATGAATTGGATGATGAAACAAA
 GTGGTATGGGAGTTCACAGCGAGTAAGAGATGCCTAGAAGAGATGAAGA
 AGGAGATGGTATAGGGTAGTGGTTCTCAATTCTGGTCCATGGTGGACTC
 ACCTGGGACCTTAAATGTACCGTGGAGGATCCAGCCAAGAGATT
 TGTATGACTGGTCTAACAGATGTGGTCTGGCACCAGGTGATCCCAGTGTG
 AGCCAGGCCTGAGGCCACTGGATTGGTGGTAAATGAGGTAACTATCAAG
 GGTACAGACGTTGGTGCACAGGCTGGGCTGAATTAAAGCTTGTG
 ACTGACTTGTGTCCTCGTGCACTCGTTGAGCCTGTTCTCAGCTGA
 GAGATGGGTGTGATAACACCTACCTGCTGTAGTTGTTGAGAGTTAGAG
 GAGATAAGCATGTTCTGGAATGAAGTGTGTTCTTAATCCATCATAGTT
 TTTGCTTGTGTTGTTGTTGTTGTTGTTCTTCAAGAATGA
 GGTTGAGCCAGACTTGTACAGCTGGTGGGAAGTGAACATGTGGTATTG
 GGAGAGAAGGGCAGTTATGTGAAGGGAATGTAATAATTAGAGAGTGGG
 GTGGGAAGACATGCTGGGAGAGTGGAGCAGGCCGGTTAGCCCTGGTAGAG
 GGTGCAAGAGAGCAGTGCAGGAACTGCCAGGGAGACAGGTGGTGGACCAG
 GGTGCCAAGGGTGTGGCTTCCAGGTCCATGGACACAGCCATCCTC
 CCAGATGCCAGCCTAGCTGTGAGTGAGCAAGAGTCTGGATTGCTCTC
 TCACTCTGTCTTTCTCTCATTCAGAAACAAAGCAGTGACTGGTACTT
 AGGAGGAGAACAGGTCAAGTTGGAGAAACTGCTCTGCTCAGGGAG
 CAGAAGCAAGAACATGGAGGCCACCCATGCTGGAAGATGATGAGGGTTT
 GGTTAGGGAGGAGGAATTGGGATCTAAAGGGGCTGGGAGTGGG
 AGGACCTGCCTAGGACAGGTAGAAACATTCTATAAAAATGGGTG
 GAGGTTGATGGTAGGACAGGCATCTTAGTTGGCTCCCTGGAGTGTCAA
 GCCCTTGAGATGGTCTTAAAGCCATGCACTGGGTTGAATCTGGTGT
 TCAAGCTCATAGTTTAAACATAATGACACTTGGAAACTATTGGGAGA
 GCTCAAGTGAGTGGCCTGGAAGTTCTGTGTTGGCAGGAGGTGACTTAG
 GATGTGCTGCTCCAGACTCATATCTTGACTGCACACCTGATGCTTCATC
 TGGCTATCCTGTAAGCACCTCAACTAACATGTCCTACACAGAACCTT
 GATATTCTGTCCTCCCCAGTCTCAGTTACCAAATGTTCTCC
 AGTTACCAATTGCTCAAGTAAAAATCTAAGTCCTCTCTGGATTCT
 GCCTGTCCTCAACATCCCACCTATCCATGAGTGTCTGTGGCCCTGC
 CTCTGAAATAAACTCTGCCCTTGCTCCAGTTCACTCCAGGCCACCCATC
 CTGGGCTGCACCCCTCCCTCCAAGCCCTCTCCCTTCTGGTG
 CTGCCTGTCATGTCAAGCATATGCATCAGTGCAGGCCAGGACATTGAAAT
 GCAACCAGTACAATTGGCGCGGTTATGCCAACCTTCTTCACTTGCAAC
 ACATTATATTATGTTGAAAGCATGCCACCTTCTCACTTGCAAC
 TTGACAGATTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGT
 TAATTGTTTGCACATGTAGCTTAAATTATTCTCATTATCATTATAGG
 AGTTATTCTTGTAAAGGGTAACTGAGTTTCCAAAACAAACAGAAATT
 GGGGTGGGCCCATGGAGCGTGACTIONGAAATCAGATTCTTAGAAGGACC
 TCGGCAAGTCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGT
 GTGTCCTGCCCTTATGAGGCCACACTGTTCAATGCTTGCCTGCAGCAT
 TACTTGCTAGGTAGTGTGTTCTACTGAACTGTCAGGGATCCAATT
 TTTGGTCTAAGTAACAAACTCAGATTACAAGGAATTGATTATAAG
 CCAGAATGCCAATGTATTACATTGGATGAAGACCATATTACAGTGAT
 TGTATCTGCTCAAGCTAAATTAGGATTAGAGTTCTGACAAATACATG
 TGAGAAGTATGAGGTTAAACTTGAATTGGACTTTCTAGAAAATCT

FIG. 4 (25 of 61)

79/118

GAATGTGATTGCCATTACATACCTTCTGGGGATGATGATTCTGTACT
 TTTATTTAAAAGACATAGAAAACATACTTAAGAATCAGATTGCTGGCT
 GGGCACAGTGGCTCATGCCTGTAATGCCAGCACTTGGGAGGCCAAGGTG
 AGTGGATTGCTTGAGCTCAGGAGTTGAGATCAGCCTGGCAACATGGT
 AAATCCCACATCTACAAAAAAACAAAAAAACAAAAAAACACCAACCAAAA
 AGAATAAATTAGCTAGGTGATGGTGCCTGCTGTAGTTCCAGCTACTT
 GGGAGGATGAGGTGGAAGAATTGCTTGAGCCCAGGAGGTGGAGGTTCA
 TGAGCTGGGTTGCAACAGTGTACTCCAGCCTGGCGATAGAGTGAGACT
 CCGCTCAAAAAAAACATCAGATTGCTTATTGCTGGTTCTTCT
 AAAACTGAGATTGGTCCCCATCATCCCCGGCCCCATTGGTAATGGTT
 CCTCCTTGTCTATTGAATAAAACAGATGTCGCTTTGGCAACATGG
 TTGAATGTAGACACTGCAGGGCTTCTGACTCAAATGATTAGGCTTA
 GATAAAACACATTGAAATGCATTCTGATTACACACCAAGGAAAGGAG
 ATCTCTTAAATCCCCTTCTGTTCCCCCTCCACCCCCCTCCAATTGG
 GCTTAAGTAAGAAGGGTGGTTACCCGCTAGTAAACCCCTTCGAAGGGGG
 TCTTCTCCTCTAAGGGAAAACCCTGTTTGACATTGCTTCATGGGCC
 CTGTATTGTTGTCCTGCTAACGGTGCTAACACAGGGCCTCCTCTT

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AAGGCTTTAGAATATTGCACACTTAGAAATGAAATGTTTGGGG
 GCGAGTTGCTTAAATATTCTTTCTAGCTTGTCGACATCCTTGA
 AAGCAGCAATTCTGGCTTGTGAGAGATGGTAATGCCCTGCAGGTGT
 GGACCAAGTGCCTCCCTCCTACATGCACGGCCCCAGCTGGGCCA
 GCAGAGTGTGTTACAGAATAATTCCAAGGGCTGTGTCCTAACCTTG
 GTCTTGTCCCCATTGCTGTAGATTGGCAATTGACTTCATAAGTGCCT
 CTTATGAACATAGATGTTGCAATGGAAGTTGAGGACAGTCAGTGGTG
 TTTTATTGAACACACAGCTAAATCCAACACAATGCTGACCTAACAGAA
 TTCCAGCCACTCTGATTCTCAGTCTTTATCTGAAAGGGTTCTGTC
 CACTTTTCCCAGATCAAATGTCCTGCAGCTACTCAGCAGAGCTGTG
 CAACTTATACGTAGAAGAGGTAAACAGTCCACAAACAGAAAGGCACAGGAC
 GAGAGTGGTCTGGGTGATGCTCCTGTGGGGAAAAGGTGATGAGGGTGC
 ATCTGCACACCTATGTTCATAGGTAAGTCTGGGAGGGAGGTGACCTCCCCT
 TTGGTTGAGGTGCTGAGGGCTTGTAGAATGGCACTATTCCATTATC
 TGATGCAGTCTGTGGAAATTGTGGTATGGCACCACAGGTACCATGCT
 GGGAAACATGCCAGATACTGCCTGCTAAGCCACAGCATGAGTCACATGAG
 CATTGTGGGCTTGGAACTAAAGTTATTGAACGATAGTTATCTGAAA
 GGAATTAGGGAAAAGGGACTTACTGCCAGGAAACAGTTGCAACACCAGG
 GGGAAAGGCAGCCTCAGCGTAAATGAAGACGTGTGCCCCAATAACA
 AAGGGAGAGTTGTCTTTAGAGAGTAAATGTCACGCCAAGGTTCCACTT
 AGGCAATGAAAGATGCAAACACTGCTTAGTTGATTTGTTACATTGC
 TGAATTGGGATTGGTCCGTGCAGGCCCTTCTGGAAACTCCAAATACATGT
 ATGACCTCTAGTCATACATGGCAAATGGCCGCTGGCTTAATTGAATT
 TAGGCCAGTTAGTCACTCAGGATTAACCTTTCTAGGGTACAGCTCT
 GAACAAATGGACTTAGACCTGCAGGACATAACTGTTCTAACCTGGAC
 TACCTGTGCCCTTGTACTGTGCCAGTGAGCAGCTGTGGCTCTGGGCCA
 GACCCACAGGGCGATAAGGCACAGAGGTACGCATGGAGCAGGCTGTG
 GCTGAGTGATCATGAAGATAACTTACATAGAGCAGCACTTTCTTCCA
 GTCTTGTGATTAACCTATTAGATCCTTATAACAAGAGTCAGTCTCTA
 TTAAACCATGAAGCACAGGTGGAGTCCAAGCTTAGTTGTGAAGGATGA
 GCCAAAAGGATTCTCTGTAGACCTCAAGCTCAGCTCTCTCATGG
 CCCTGGAGTAGGTGAGAAGGCCTGTCTTCAGAGCCCAGCCTGCAATCA
 TCTACATTCTGTTAGCCAACTCTAGGACATTGCTTACCAACTGAAG
 GGTGAGAACTATCATAAGTTATAAAACAAATTGAAAACAAAAGGTAC
 AGAACAGAAAATAAAAGATGAGAATCTATTAAACATAGTGTACTGG
 AAAAGGGGGCTCAAACCAAGACCCCAAGAGAGAGTCCTGGATTTCACAC
 AGGAAAGAACTCAAGGTGAGTTGCAGGGTGGCTGAATTGAGAGAGTTA
 TTGAAAGCTATTCCATTACAAAGTAGAGCATCCTCAGACAGCAAGTGGAG
 GAACATGCCATATTAAATTTCTTATATAGGAATCTGTCTATATAAA
 GACTAAACTAAGCTGTGGCTATGTGTGGGTGGGCCAGCATGAAAACA
 TTTATTCTCCTATTGATTAAAGAGAACTATCCTGACATTAGTGTGT

FIG. 4 (26 of 61)

80/118

TTAAGTACATCAAAGCAAACTATAATTATCTGAAAGCATATATTTTA
 TAGGGATTGGGACATCTGGCTTCTGTGTTAGAAGTTGTCTTC
 AGGGATTACCAAGCCACTTCTTAGCTGAAACATCTTAGGGCATGGT
 CCTGACTGGCAAGGAATGTGCTTGCTAGTTTAAGATGGGCTTGATTG
 AAAATGGTGTCCATCTGGCTCCTAGGCTCTGCTTCCTAACAGTAAG
 GGTAAATGCTATGTTATGAAATGTCATTCTGCCTTAGCTGCAAACCTC
 TTGATGGTGAATTCTCTGTCCGTTTCAGTGGGTATTTATTCTGCAT
 CCACGTCTTCACAAGGAGCTGAAAACAAATTGGATGGAAGCAACTGGGTT
 TTATGGGACACGTTAATGTCATTGGTGTGGAATTAGATGT
 CCAAGCAACATTTACACTACAAATCGCAACTTTAACATCACTCAAAG
 TACCTGAACCTCAATGCTTCAGACAGACTTGGTATAAGCCACCACCTC
 TTTCTATTATGGCAGGCCATCCTGAGGACACAAATTCTGCAGGGCTTC
 TGGCATACTCTGATTAAACAAATGTCAACAAAGTTAAAACAAATGT
 CTCTGATTGTTAAAGCCTGGATTTACTCATTGAATATTCACT
 CCTACTAGCATGTTGAGTAGTTCTCAGGGACCTAATTATTGCT
 ATTAAAAATATGTGTCAGCTACATGTTTTTTTATCAATPTGCAATG
 AAAACTTAATTGAATAATCTATTAGTGTATTATTGAAAGTGAATCT
 TTTCTTTGCTTCTTGTCTCACACATAGTGCAGACAGTTCCACACG
 GGCTCATAAAAGAATGATTCTGCCTTGTGAACTTTGCCTTATTG
 TTAATTGCACCAATTGTGACTGGCTTCTGACCCCTGTTGTAACCAAGCT
 CATAATGTACATTATTCTTATTGCAAGTGTAGACACTTGAAGGAAAGTT
 CCCATTCTTGTCTTCTTGTCTTGTGATAACTTTTCATG
 CAGACATTCCCCCTTTTTTTGAGACCGAGTCTGCTCTGCATC
 CAGGCTGGAGTGCAGTGCATGATCTGGCTACTGCAACCTCTGCCTCC
 CAGGTTCAAGAGATTCTCTGCTTCAGCTTCTAGTAGCTAGGATTGCA
 GGCCTGCACTACACACCCAGCTAAATTCTCAAATTAGCCACCCACCT
 GGCTAATTGTTGTTAGTTAGTAGAGACAGGGTTCAACCATGTTGCCA
 GGCTGGTCTCGACCAGGTGATCCACCCGCTTAGCCTCGCATAGTTGAG
 GTGCTATTCTGAGCTCAGGGCTCTGGCAGCTACAAGCCAAAGATGCGGTC
 TCCAACATGTGCCATTCAATGTCATGGCCCTCTACTGGCTCTGGAA
 GCGCAGCTCTGCCAGTAGCTCCAGCAGGGCACAGCTGTTAAGTCGTGATG
 TTCTACAGGTGACCAAGGGCAATCTCTGGACTCCTTAGCCGCTAGGTCC
 TCTCTGTAGCAGGACCCAGGAGAAGGCAGGGCTGAGGATGGCTCTCTTA
 GACATTGATGAAACAAACGCTGTCATTGAAACTCTGTGAGCAA
 GCAGGTGAGTAGAGTTGGTTATAAAAGCTTAGGGCTCACTACAGAG
 ATGGACTTGCTGTGAGATGGTGCAGAGCCGCTGAAGAGTTCTACTTGGG
 GTAATGGTGTGATTGGTTTGGCTTGTAGGAAGATTCTTGGCCAGAATG
 AGGCAGGCAACCCAGAGCAGGGAGTGGCCACATGTGGGTGTGAGTTATG
 GGCCACTAATCCAGGTGATAAAATGGTGTCTGAACTTCAGGTGGGCTG
 CCACATGTCTCCATCTGCTCTGACCCCTTGAGACTGGCCTATGGGCTGC
 CTTAGGGCTCTGGCTCTATCTCTGGTGGCTCAGGCAATGGGAG
 ATCAGAGGGAGGAAAGAGAGCTTGGTTAGAGTGCACCCGGCCCTTCAG
 GTTGGCAGTGGCCACATTCCCCTATACAGAAGGGCACAGTTCTGTCAGT
 GGGCCCTCCCACAGCCCCAGCTTCTCAGTGGCCAGCCACCTCCCCATCC
 CTTGGCAGCTCCACCATCTCTGCTGCTCTCTGGACCTGCTGCACTGTT
 TATAAAATAACCTTCTACATTACCTCTAGCATGCAACCTTTGTGTA
 TACTCTGCCCTCTGTCAGCACATGACTCATGCCAAAGAGTTGAAATT
 TTCTCCAGGCAACGGGAGGTCACTGGAGGATTAGACATTGAGAACAGA
 TGTGTTAGTGTGAAATATCTGCTGACTGAAGTGCAGCAGGATGGTCAA
 AGAGCGAGAATTGAGGCAAGCAAACCATCAGCAGGCCAGCAGCAGAAAT
 CCAGGTCAAAACAGGGAGCTGAGGCTCACAGGGTTGGATCAGGGAATG
 GGAGAGGGAGCCAACAAATTCCATGAGCATGTCAGTTGCACATATGACT
 TGGTAACATTGTTATTGTTATGTTGAGACAGAGTCTCGCTC
 TGTACACAGGCCAGAGTGTAGTGGCATGATCACAGCTCTGCAACCTC
 TGCCTCTAGGTTCAAACATTCTCTGCTGCTCAACCTCCAGGTAGCTGG
 GACTACAGGTGCGCACCACACTACACCCAACTAAGTTGTGTTAGTAG
 AGATGAGCATTACGCTGTTGCTTAGACACGG
 >Contig47
 AATATTGATTATTGACCAGAAATTGACGCTAACCGTGACCCCTGGC

FIG. 4 (27 of 61)

81/115

AAAATAAAATAGTGTAT...GTACGTGCATATACATGCAAAGAAATGAG...
 GAAACTAGAAGGATGTCATCAAATGATAACATGGTCATCTGGGGTCGG
 AGTACATTGGGGATGAGGGAGCTGTAAGCAGACTTGGACCTTTCT
 TCTACCACTACCGTGTCAATTGAATTGGAAAGAAAAAAACTCAG
 AAGGAGGAGAAGGAGCAGGAGGAAGAAGATGGATCTAAGTGATTGC
 CGGGAGCACCTGAGAAGGTGAGATTCAAGTCTAGGCTAAGCTTCTA
 ATTCCATGAGTGGGAGTGACCCACGTCCAAGAGGAAGCTCAAAGGAAGA
 TGTTCTCCATCATCTCTGCTCATCCTAACAGCATGCAAACACATCCA
 ATGCAGCTCAGAAAACCTCCAAATTGCCAATTGCAATTGAAACACTTAA
 TGCTGTGGTTCCAATTCAACTGTAAAGTAGGTATGCAATTGTTA
 CCATTAACCTCTCAGAAATGGAGAGAGCTCTTCCGCTCCTCCCCCT
 CTGCTGTGGCTTGGTGGAGACGTGCACTCAGGCTCACCTGTCATGAT
 CTCCAGTAAGTACACATGAGCAGAGAGGCCTCAGCTCAGCTTCCGT
 CCCACCAGGGTGTGATTCTTGAGAATTCTAGAAATGCCACATCTAGGCC
 CCCAAAGAAATCCTGCATCTTACCCCCAGAAATATGAATCATAGCAAATT
 TCAAATCAACCACGTTTAATACTCACAGACTGGGCACATCCAAAACAT
 ATTTTCAGTTTACAACAGTGCCTGGTCATATCGGCACATTGTTGGAA
 GCAATAAAATCGACACGGAGCTGAAACACAAACAAATGCCAATTGTTT
 ATAACACCTGATTTCTTCTGTTCTTATGAGTTAGTTGTTGTTG
 CTTAACTCTACCTCAGACCATAGTCTGGTAAACTCACCACCCAGAAGCTC
 CCTTGAAATGTGGGTATGCCACTAGGTGGCAGGAGAGATTCTG
 CTGGAGGGAGGACAGCCACTCTGCCCCGGGTCAAGGCCAGGGCACCC
 CTACCTGAAAATTAGCATGGGCTTATGAACCACAGCTTCTAATAAA
 CACAGGATCTGTTGATAGAGACTCCAAAACACGCCACCTAGTGTGAA
 AGACTCAACTTCAGAAGAAAACCTCATGGCAAACATCTCAGAGATGTT
 TCCAACCTTAAGGTTCTGAAACACAGACGCTCCCCAGAAAGCCATTGTT
 TCAGCACCTGGGAGCCTGCTTCTGCTTACAGACTCGCTGTTCTTA
 AATCACTGCCAAGATAACATCTGCTCTCTTACCCCTTATTCGATA
 TAAGGACTCCTCACTCTGTTGCTTCTATTGGCTACCTCTCCACAGGG
 GAAATCGCTGATTTAACAGCAGTCAATATCCAAATCTGGAACAGGGAA
 AGGGAAAGCATTAAAAATTGGAGAATTAGGCCGGCACAGTGGCTCATG
 CCTGTAATCTCAGCACTTGGGAGGTCGACGGTGGATGGACTACTTAGG
 TTGAGACCAAGCCTGGCAACATGGGAAACCTCATCTCAGACAGATGTT
 AAAAAAAAAAAAAACCAAAATTAGGCCGGCATGGTA
 GTGCACACCTGTGAGCCCCAGCTACTCAGGAGGCTGAGGTGGCAAGACTG
 CTTGAGCCCTGAGGTCGAGGCTGAGTGGAGATCACACCACTGCAC
 TTCAGCCTGGCAACAGAGTGGAGACCTTGTCCCAGATAAAATAATTAA
 TAATTAAATTAGAGGATTTAAGGATTCTTCTTACAGACACCTCTTATTT
 TCTCTGGCTTTCTGACTACTCTCCCTAACTCCCTGCTCTGGTCTC
 CCAAAACTACTCCAGAAAAAAAGGGGGGGAGGGACTAAAGGAAAGCC
 AGGTGACAGTGCCTGAGATGACAAGCATCTGCCGAACAAACC
 GTAGGTCCCTGAACCTCTCCAAGACCTGCTGTGGACTTACCTATGAAA
 ACCAGTTTAGCAAAACCCCTCTAAGCCAGTTATCAAGATCCCTTAT
 CCTCAATATCCATCTGATTGGATTCTCATCCCCCACCATTCCCCAGTGA
 TGTCAACAGGCCCTTCTCAGCAACAGTAGTTAGTGGGTGTAGCCAGGAC
 GCCCCCTCACCCCTGATATGCCCTTTAGTAATTCTCATCCACAGGTT
 CCACCCCTGCTCTAGGCTATACATTCCATTGCCATGCTGCATTGGA
 ATTGAGCCCAGTTCTATACTGAGGTCTTACTTCACCTCTGCCATAGTCC
 TGAATAAAATTGGTTTACATTAAAAACTGTCCAGCTCTGGTTGTTCC
 TTGACACAGGGTAATTCTTATTCCATGTGATAGTTGCCTTACCTCAGCC
 TACACCCCTCAAACCTGCAACTCTATATTCAAGAACCCAGACAGCC
 CAACAGATAGGAAGAGGCTGCCCTGGTCAAGGAAGGAAGAGGCTGGGAGG
 AAGGAGAGAACCCGAAGGCTGCCCTCTAGACTGAGCTCTGGGATG
 GGTGGACGATAAAACCCAGATACGTTAGACATCTGAGCGTGGAGAGGAC
 TTTGCTTGCTTCCACAGGGACCCCAAGGAAACTGCAAGCCCTCCAGAGA
 CTAAAAACAGCAGAACAGCAAGAAATGGCAGCAAAGGTCTGGGAGAATC
 ATCCATATGTGGGACAGACACAAACAGACTCCCTGTTGGCCCCAGGAGG
 TTTAAAGAAGATCCAGAGGCTGCTCTATTCCATATCTCAGCAGAGACAGG
 CCCGTGAGCCTAAAGCTGATCATTAGGACAAGAAGGACACGAACACTGTC
 TGCAGCGTGAACCGCGTGGAAACAAGGCCAATCACCAGACACCAAGACCAGC

FIG. 4 (28 of 61)

82/118

CAGACACAGCCCCGAGTCCCCAAGACCAACCAACGGACCCATCGCCCCCTC
 ACCAATAGCTCCAGGCTACATAGACCCCTCACTTCATGGATGTCCTCA
 GAGCAGAAAGGGGAGGCAGGAGTGGAACCCCTGACTTGGGTCAGTTGAAAC
 ATAAAATGACTGTACTATTATTGAATTGCTGAAGTTACGTGAAAGAAAT
 GAGATTTAGTTTG GCCACAGT GCAA AATAAGA AACGAGGCTCAACTG
 AGATTAAGGTGAGTTAGGAAATG TACTCCCTGAAGGACCTGTGAAG
 TG TGT CGCTATGAGAAATGACCAGAATCCACGTTCTAGCTGCGGGAC
 TCAGGCTGACTCCTGTTCTGGAGCTTGACAAAGGGCAGGGAAATCCCT
 GTTTCAGGCACAGTGATTCAATGTTAAAAGAAAACAGGTGGGCCCTGG
 CAATCATGATAACATGTCATAAGTTACATCTGTGAGGCAGGTAGTGT
 AATCCCATTGCAAAGGAGGAAACCGAGGCTGAAAGCAGCTACATGGT
 CTCTTCATGTGGCCCAAATGTTGGAGAACAGAGCTTAAC TGAAATCAGCA
 ATTCTATACCTAGAACACTGACTCTCTTATTATATCTCACTACACCTT
 GATATTGAAATATTCAACTTTCAATCAAAAAATAACAATAATTAG
 GCATAATGACTACTATGTCATTAAATTCTGCTGATATTCAATATCCC
 ATGCCAGGAATATTGAAAGCTCAGCTCCTTAAGAGCTGACTATGGCATCA
 ACTCCAACAACCATCCTCCAGAAATATTCCCCCTTCTTTGTTATA
 GAGTGGCACTGCCCTATATGGT GACCCTTGCCACATGTGGCTGTTGAAC
 ACTT GAAATTGGCTTGT CAGAATTGCA GTG TAAAGTGTAAAACACATACC
 AAATTCAAAGACATGGCACATAATAAAAAATG TAAATATCTCATTAAAC
 AATT TTATATTGACTGTGTAAGTAA CATTG AATATATTGGATTAAAT
 ACATGGATGATGCCCAACACCCACAGTCCCTTATCAAGTCTCTACTTCA
 CATT TTG TACTTCTGACTTAGAAATAGCACTGGCGTCAAGAGCCTATT
 AATGTCGTCAATAGGTTCTGGGAAACCACAATTAAACAAAATGACATA
 TAAGAAAACGAAATAACATTGAAACAAAATGACATTATTGAGGACTGCTG
 CATGTTGTTCACTTAAAGTCAGTGTCCAAGAACCTATCAGTGACATT
 GTGAGGACTTGTCTCCTCTGTTACAGGAACCTGGCAAGTTACTTA
 ATTCCCTCTAACGCTGGTTATATCCCTGCAAAGAGAGAAGGATAATAAC
 ACCAGTACTTAGTGTGTAAGGAGAAAATAAAATAATAAAATATGAAA
 TGGCTGACAGTGTCTTGTCAACACAGAAGATGTGATCCACAGTAGCTG
 CTATTGTCGCTCACTTCACTAGTAATGGTCCAGGGAGGCTTTAATGT
 GCATGGTGCAGTACATTGACATGTTGGACATGGGTGAAGGGAAAGACCAG
 GCTCATCTAAACACAATAGGATGCTGTGGTGTGGAGGAGGAAATCAAG
 GACTAGTTATCCACAGCTGTAACATGCA TGATGAAAGAGATAAGGCAC
 ACAAAAGACTTGTCA GTAGCAAGCATTACAAAATGCAAGAGACAGCTG
 TGGGTGGTGGTGA GTCA GACCCAGCTTCCCTGTGCTGGCTGAGTGGT
 TCTGGCAAGTCACGCCATCTGCTGATGCCCTTCCCATCTATAGAGA
 GGGAGCAACTGAGGCCCTTCCAATACTGAAAGTCTTATTCTGCTACT
 TTAGAAATATCCACATTGTTGGTAAATTCAAATGATCCAATGATTCCATT
 TCCTAATGTTCAAACACTAGCCCCAGAAACATCTAAATGAATCAAACAAAT
 AAAATTTATTTGTTGATGTTGATTGCTGAAACTCTTATTTAGCAAC
 ACACACACACACAGAACCCATAAGCCTCATCTTCCCTGGATAAA
 CGAGCCTTCTGTCTGGCCATTAGTCAGGATTAAGTAAATGATTCCA
 ACTCGCCTTTGCA CGACTGAGCTCAGATGGTCTTCTGCGTGGCAGTGGCC
 CTCCCTGACTTATGATTCCCTGTGTGTCGGCGTGTACACTGCAGCTAA
 CTGAGGAAACAAGAACAAAAGACTGCTGACCCCAAGAGAGACTGTTGGAGG
 CAAAGGCTCAGTCCAAGAACCTCACACGTGGGAGCCGAGAGCCCAG
 CCCTGACCTTCTCCAGTAATAACATAAGAAACACAGGACTGGCCTT
 ATTGGAACAAAGAGTGGTGTGTTCTTAAATCTCCTTGTAGTCAGG
 GCTACCCCTTCATGGACGCCAACATCCATGGTCTGCTTGAGTCCCT
 GCTTCCATATTCTGCACTTCTCACTTGAAATATCCCTGGAGTACGTTAA
 GCAGCCAGGTTGGAGTTCTGCTGTGCA GGCGGGTGTGCA TGATGTCCT
 CTCTCTCAACAGGACACAAGCTCCCAAATCAGACGGTATGCCTCACGC
 CCCTTCCCAAGCCTCCCAAGCAGCACCGAGCATGTGAGGGGAGCTGGGC
 CCAGGCCATGATGGGAAGCACTCTGCTAAAGACTAGGGTGTGCGC
 CTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTGCGCTCGGTTTCT
 CCTGGACAATCAACATGAACTCCTCACCCCTTATCCACTTGCATAAA
 CTGAAAATAACAAACCCAGGGCTTTCTGTCAAGGAAAGGGTTTTT
 TTATAAAAATTAACAGAGATGATTCAACACACCCAGGATAAACACATGG
 GCCATGAATCAAGGGCAGCATTGCTCTGGTCA GCGCTGTTGGGCC

FIG. 4 (29 of 61)

83/118

CTTGGCAGGGCTCCCLTGAATCTCCCTCTGACTCCCACAC
 GCACTCCANCTTGTGTTACAGGCATAAATGGAAAGGGTAAAT
 >Contig48
 CATTCTTAATTAGAGAAACGCTCATTAACCTAGACACCCAAATTCTCTGG
 GGGGGGATCATTCTACAAGCATGCCCTCTCTTAAAGAGAGAGCACT
 TTTTCGCAAATAATGCTGCCATGAACATACGGGGTGCATGTATCTCGT
 AAAGAACATGATTCTATTGGGGGTATGTACCCAGCAATAGGATTGCT
 GGGTCAAATGGTATTCGGTCTAGATCTCGAGATCTCCACACCGTC
 TTCCACAATGGTGAACTAATTACATTCACATTCTACCAACAGTGTGAAAGCAT
 TCCTATTTCTGCAACCTGCCAGCACCTGTTATTCTTGACTTTAA
 TAATCGTCATTCTGACTAGCATGAGAGACAGTATCTCGTTGAGGATTGA
 TGTGCAATTGCTAATGATCAGTGTGAGCTTTTCATATGTTT
 TTGGCTGCAAGAACATGTCTCTTGAGAAGTGTCTGTTCATGTCCTTGC
 CCACTTTTAATGGGGTTGTTCTTGAAATTGTTAACGCTCCT
 TATAGACTACAATAACAAAGACATGGGATCAACCTAAATGTCCATCAAT
 GATAAACGGATAAAGAAAATGGTACATATATACCATGGAATAGTATG
 CAGCCATAAAAAGAACATGGGATCATATCTTGTGAAAGGACATGGATGAGC
 TGGAAACCATGATCCTCAGCAAACATGCAAGAACAGAAAACATTGTTG
 CATGCTCTCACTTATAAGTGGAGCTGAAACACTGAGAACACAGGGACACA
 GAGAGGGAAACACACATTTGGGCTGTGAGGGTGAGGTGGGGAG
 GGAGAGCATTAGAAAAATAGCTAATGCACTGCTGGCTTAATACCTAGGT
 GATGGGTTGACAGGTGCAAGCAAATCACTGTGGCACACATTACCTATGTA
 ACAAAACCTGCACATCCTGCACACGTACCCAGGACTTCAAATAAGAGA
 GACAATACTTCTCCCTTAAGTGTCTACTGTTGCTTGCAATAAAACTTC
 CTGCCCTTCACCTCACTGACTTGTCCCTGAAATTCTTCTGATGGT
 GTCAAGAACGTGGACACTGGCTGGGCTGGAGACTCACCAGCATCCGGAG
 ACCCTCCTGAGCCCTCCAGCAATAACACTTGCACAAACTATGAAACTA
 CAGATCCAAGAACGCTCAAAGAACCCAAAGCACAGGAAACATGATGAAACTA
 CATGAAGGAACATCAGAAATTGAATTGTTCAAATCAGTGTAAAGAGTAA
 ATCTTAAAGCAACCAGAAACAAATATCCATCATACGCAAGAAATAAG
 ATAAGTATGACAGCAGATTACAAATAGAAAAAAACAAAGTGCAGCAAC
 AGAAACAAACTATCAATCCATAATTCTATACCTAGTGAATTTCTTCA
 AAACAAAGGTGAAATAAAAATTATTCAGGAATACAAAAGCGAAAAA
 ATTAATCACTAGCATTCACTGCAAGAAATGTTAAAGGAAGTCTTTA
 GGCAGAAAGAAAATGATACAAGGTGAATATTGGATCCCTGCAAGGAAC
 AAAAGATCCAGAACTGATAACTTAATGGTAAACATGTAATTTCATCA
 ACAAGTGAATGAAATAACAAATCATGATATATCCATATGATAGACTACTA
 CTTAGAATACAAAAGAACAAACTACTTATGCACTGATGATAACATGAAATGATA
 TTCAAAATTATTATGAGTGAAAGACACCAGATCAAACAAAGTACATAC
 TGTATGATTGTTATATAAAACTCTATAAAATTGCACTGCTCTCTATAG
 TGACAGAAAGAACATGAGTGGCTGCTGCAAGACAGGAAGAGATTACAAAC
 GGAAATGAGAAATTCTTAAGAGATGATGGACATGCTCATTACCCATCATA
 TGTATACAGCCATAATGGTTTACAGATAACATATATGTAACGCCAAC
 ATAAATATAAGTTATCAAATTACAGTAAGTGTCTGACTTAATGTCAGTAG
 TTCTGGAAACTTGACTTAAAGCAAATGAIGTACAGTGAACCAATT
 TACCATAGGCTAATTGATATAAGATGAGTTAGGTTTGGTTTTTT
 TTTGACATGAAGTCTGCTCTATGCCAGGAGAAGAAGAGTTAG
 GTTTACAGCATGTTCTGGTCAACAGAACATCATCAAACATTGTAATAA
 AGGCACAAACACTCTAATATTAATATCAAATAATGAGTTATAC
 AGAATTAAAGAAAGATTAATAAAACAAAGTAAATCATTATTTATGGGAT
 TTTGGTAATCAGTGAGTTATGTGTCATAGTGAAGTGGTTAAGTCAA
 GAAATAATGTTGCAAAACAAAATTAAAGATCCTCTCCTACCA
 CACAAAAACAGAAAACCGTGGCTGCTAACGACTTTGTACCA
 CGTATCTTATGCGTTGTATGATTATTGTAATGCTTATGATAATT
 AGAGACAGGGTCTCACTCTGTGTCAGGCTGGAGTGAAGTGGTGC
 ATAGCTCACTGCACTCAACCTCCGGATTCAAGAGATCCTCCACCTC
 AGCCTCCAGTGTAGCTAGGACTACAGTTGTGTCGCCACCATGCC
 CTTCTTTTATTGAGAGACAGGGGTGTGCTTGTGCCCCAGGC
 TAGTCTCAACTCCTGGCTCAAGCAATCCTCTGCCAGCAGCAC
 ATGCTGGGATTTCGGACATGAGCCAGCAGCACCTGCCAGCATT
 ATT

FIG. 4 (30 of 61)

84/118

TCATAATAATTATAAGTCATTCCTTCATTCATCTTACAACCCACCTGGTC
 CAGTTCAAGGATCTCGGGTGAACAGAACCTATTAACGTTCACGCACAAGTC
 AGAAACCAGCCCTGGACAGGACACCATCCTACCGCAGGGAGAACCTACAC
 ACCCACACTCACTCAGACTGGGACCATGCAAAGAACCTAACGTGCACTTT
 GGAATGTGTGTTCCATACCCACTAGAACAGCTAAAATTAAAAGACTGAC
 CATACTTGAGTGTGAACAGGATGTGACACAACCTAAATTAAAGCGCT
 TCGCGTAAATGGCACAGCGCTTGGAAAACAGTTGGCAGTTTCAG
 TTAAATAACCCAAACTCTATGATCCACTCTCAACAAATCAAACAAAGAGA
 AATAAAAGCAATGTCTACACAAAGATGTATACACAAATGTTCAATTGCA
 CTTAATTATACTAGCCCCAAGTTGAAACAAGCCAAATGTCCATTACAGA
 TGACTGGAACATACAAATTGTGGTATATTGATACAATGAAATACTACTTA
 GTAATAAAAAGAAAGAGCTTAAACATAAGCAACAAACATGGATGAATCT
 GAAAACAATTATGCTAAGTAAAAACAGCCACACAAAGTTACATACTGTA
 TGATCACATCTACATAAAATTACAGAAAAGGCAAACATCTATAGACAG
 AAAAGCAGATGAGTGGTACCTAGGGATGGGCAGAAGGGACGAAAGGAT
 GGATTGAAAATAGCACA AAAATTGGAGGGATGACAAATATATTCA
 ATCTTGATTGTGGGATAGTTAATGGGTATATAGAGATCAAAGCTCA
 TCTAATTATACTTTAAATATATGTATTTCATTGTGCATCAGTTATTCA
 TCAACAAGACTATAAAATAATATATGCCTACATACATTAAATATTCA
 AAATCTCACAGTTATATACATAATGCAACTGAATATGTATTCA
 TTAACAAGCAGAAAGGACTGATTAACATGACAGCGGCTTTCTGGG
 AAGGGTAGGGAGACAAGAGATGGAAAAGAGGATGAGAGCCAGAAGAGAC
 CCTTGTAAATGTTCTTCTTTAGTAAAATATATTGACAGTTAAAGCT
 GAGAGGTGAGAATAATAGCTCATGGCTTTGTGCCTTAAATTCACA
 AACTAAGTGAAATGGGAGAAAGCAAAAAATAAACTTAAATAATGTTAT
 ATTGCCAAAAGAGATTAAAATGGAGGTAGACACATGAGACTTACGT
 TCTAAAAAGTAGAATCTGAGGGAAAGTTAACAACTATAAGAATTAA
 AATCTAGCTTCTACCAGCCAAAGCCTAAAATGTTCTGCTTATTCTCC
 TTATTATAATTCTAGGTAATATAATTATGTTGCAAATGAATGCAGTG
 ATATTAGATCTCTAACAGGGTCTAAAATGAAAGTACATATTCCAATT
 TTCCCATTTCCTCTTTCCATGAATGAAAATATACATATTGATG
 ATTTCCAAGTTATACAAACGATCTTCTCTAGTTCTCTTACCAAAT
 TCCCTCCCTCACTCAGCCACCAGCAGTCAAACGTGCTACCTGCACAGC
 AGCCCTCATACCCTCACACTCTCATCAGGATCCTGCCTGACCTGCGAGG
 AGCAGCAGCAAGAAGGAGACAGAACCTCCACGCTGAGCATCTCAGGGCTT
 TCTCAGAGACTCCAGAGGACCCCTGATAGGGACAGAGCCTGGCCAGCAATC
 CATGCTGCCAGCTGTATGATTGTGGCATGTAATTCTCAACTGAAAATG
 GGTGTAATAATAACATGTTCTCCAGAATGAGCTTTATGAAGATCATAT
 AGCTTTGGAACTCAGACAAGCACTGGTAGGAATACAAACAGGGGAGCC
 AACAGCCTATAAAATAACTTTAAGAAAGGGCATGAATGTAATTACTTAG
 GAACAAAAGGCAAAGTGGAGAGATGCCAGGGACTGAGCTGGACAAGCTGC
 ACCCTTATGTGGCTCAGCCCATGGGCTGACAAGGAAAATGGAGGAGCTAC
 CAAAGAAGGTGAAAGGATTCTGGGAGAGTGGCCCTCACCTGCCAGGGC
 AGGGCTCAGTGGGAGAGAGGGAGATCTGTTATAAATGCTGCCAGGAGGTC
 GAGTCATGTGAGAATGTCCATGTGAAAACATCCACTGTGTATCTAAAG
 AGAGTGGCTGTAACAGGTCAAGGGTCAAAGGTCTTATTGTCTCAGATGT
 TATCTGCATGCATTGTCTCACGACCAAGAAAACTAAGGAGCATGGACACA
 AAGGGTTAGGITGAAGCAAAATTAAATAAGTGAAGAAGAAGGCTCT
 GCAGTGGAGAGGGAGTCTGAGTGGGTTGCCACTTGCACAGCTGAATCCA
 AAAGCTTTATAAGAAACTCTCTCATATCTGCAGCTGTTGAGTAACCT
 CTCTTACCTATAAAACTGTCAGTGTATAACTCTCCCTATCTATGCAGCTGT
 GGGATGTCTCCAGGTAAAGCATAAAAGTGTAGCTCTTGTGTTGTTGTTA
 GTGGGTTGTTAGGCAAGCCCCATCCCTGTGTAAGCTCCCAT
 GGAGCCCCACCATGTGCATATCTGAGAACAGGGCTCTGTGCGCTTATCTATTCA
 CTCACGTACAAAGAACAGGGCTCTGTGCGCTTATCTATTCA
 GGTGCAGCCTGAGTTTCCCAGGCTGCTCTTTGCGCTGTAGCTATG
 ATTTTCAGGCAGGCTGCTCTGTGAGACTAGCCTTAACGTCTACCTA
 TCAGATTTTCTTTCTTCTCCCTCAGCTGGTCCCTCACCAAGGCTG
 AGCAAGTGAAGAAGGAGGGCACAGGGCAGGCAAGTAGTGGAGCAGCAACAG
 GAACTAAGACACGAGAAACACTCTCACACCTGGGTTGAAAGGGTGGG

GAGCCAGGACTACAGC1 AGGTAAAGAACATAGGTAAAGAGATACTGTTGT
TGTGTTGTTTAACATATGAGAACATTGAGCTTTAATTCTACAGGAA
GGATCCAGTTAGACAGGGAGCACCAATATTAGAAGAGAACATGGT
GTAAAGGTCTGGGAAGGGCTGAGAGGATTGGGACTCAGAATCCAGAGCAG
AAGCCGTCTGTGAAACAGAAGAAGGACCTCCCCAGTGAGCAAGAGGGAG
GGAGGAGGGACAGATGCCAAGATGGTCAGGAAGAAGGTTGGTAAA
TGTGAGGCTGTGCTCACCTGCTGGCTCAATTCTCTTAAATGTCAG
ATGGAATCATTGATGAAAGGCCATGCCATGCAATGAAATGGCAGTCTGAG
GCATGGAGCAGCTCCAGCTTAGCCCGTGTAGGGTAATTATGGCTCAA
CCCAGGAGATGAAATATGACTAGGGAAAGTGAAGTCCAAAACAAATGGTC
TCAAGTTGACTGTGAGTCTCTGGAGGCTGAGACGACAGGTGGGTTGA
CAAGGGAAAGGGAAACCCACCTGCTGAAAACATCAGGCTGTTGGCTGGG
GAGGGGTGAGGCCGTGTTGAGAGATGGATGGATGCCCTAAAGTTGGGTA
AAGGTTCAACTCTACCCCTGCTGGGTGAAAATAACAAAGACCACC
CAAATGAGAACAAACAAAGACTATTATCCAGAGCTTGCTGACAAGGG
AGTCGGCAACCCTCACTTGCTTGGAGAGACTCAGAAGTAACAGGGAG
AAAGCCTCATAGCAGAAAAGAAGGGAAAGTCTCATGATGCCCTGAGTGGC
AGCTGTAGATGTGGGTGAGTTGCAGGTGGCTAAGTAAATGGGGGACTC
CTGTTGATTGATTAGGAGCATGTTGGCTTCTCTGGTTGGCTTACAT
TGGAAAGAGGGAAACAAAAAATTAGGGCAGTTGTCAGTTAAATCAAGTG
TTGGCCATTGACTGACTGTTACAGGAGTGAUTGGCTCCCTGGATTGT
TTGCTAGAAATAGTGGCTTCACTCCTGCAAGTCTGACTTTCTGGTAAT
AGGCTTCTGGGTGGCTATTGTTGAGATAATAAGTGGGTTCTGAGCTGA
TTCTGAGATTGTGGATCAGAGTTATTATATAAAACAGTCTGACCATT
TTCCACTGGCATATTCCATCTCCAAGAGCTGGCCAAGCTGCTGTCTTAT
CTGTCCTCCCCAGCCCCCTCCACTCTGGCTGTGAAAATACAAGCCACTAGG
TGAGGAATGGGACAATTGAAGACTGAAAGCTTTCTTGCTGGGTCGC
AGAGCTGAGGAAAGAAATGACAACATCCAAGTGTCTGCCCTGGCCAGTT
TTAGGACTGTAGTGGTAATGCAAGGACTGTGAGTTATTTTCAATT
GTCTCTCTAACTAAGGTGGAAAAAAAAAAACAGAAAATGTCTGCTGCA
GTCTCTGAAAAGCTAACACTGTGCTCCAACATTGCAGCCATTAGCC
ACAGGTGAGTATCAAGCACTTTAAATGAGACTGGTCAAACAGATGTG
CTCTGAGAATAAAACACACAGCAGATTCAAAGACCTAGTACATGCCCTG
ATTTCAAGCTATATTACAAAGCTGGTAATCAAACAGTATGGCATTGG
AAAAAAATAGACACATTGGCAATGTGACAGAAATAGAGAGGCCAGAAAT
AAACCCGTGCATGTATAAGTCAACTAATCTTGACAAGAGTACCAAGAATA
CACAATGGGAAAGTCTCTCAATAAGTGGTTGGAAAATAGATATC
CACATGCAAAAGAAAGAAATTAGACCCCTGTATTACACAAAATCTAAAAT
TAATTCAAATAGAAAAAGACTTACATGTAAGATCTAAAACATAAAACT
CCTAGAAGAAAACATAGGGAAAGAGCTCCTGACACTGGCATTAGCAGTA
ATTTTCAGATATAACATCAAAGTACAGGAATGAAAGCAAAACAGT
GAGAGTATATCAAACAAAAAGTTCTGCACAGCATAAACATCAACAGA
GTAAAGACATGACGTATGGAATGAGAGAAAATATTGACATCTGACAAGG
GTTAATATCCAAAATATAAGTAAATTCAACACAACAGTAAACAAAAGCC
AAATAACCTGACTTTTTAAAATGGCAAAGTACCTGAATAGGTATTG
CTCAAAAGAACATACAAATGGCAAGAGATGTATGAAAAGCTGCTTAA
CATAACTAATCATCAGAGAAATACACAAATCAAACAGATATCATCTCA
CACCTGTTAGAATGGCTATTATAAGGATAAGTGGTGGCCAGGT
GTGGAGGAAGGAAACCCCTGTACATTATTCAAGGAATGTAATTAGTA
CAGCCATTATGGAGAACAGTATGGAGATTCCCTAACAAAATTAAAAATAG
AATTACCATATGACCCAGCAATTCAACTTCAAGGAATACATTCAAATACT
ATCAGTATCTCAATAAGATACTTGCACCTCATGTTGAGCAGCGTTAT
TCACCATAGCCAAGATAACAGAAACAAGTTAAATGTCATCAACAGATAAA
TGGATAAAGAAAATCAGGTACATATATATACAAATGGAATATTATTGAG
CAAATCCTGACATCTGAGATAACCTGGATAAACCTGGAGGACATTATGC
TAAGTAAAATCAAAGCCTGACACAGAAAGACAAATACCAACATAATCTCAC
TTACATATGAAATATGAAAATGTTAATTATGAAACAGAGTAGAATGG
TAGTTGCCAGAGCCTGAGAGTAGAGAAAATGAGATGCTGTCATCAAATCAA
TCATCACATTGAAATATATATAATCTATTGTCATTAATATTAAAGAA
AAAAAAATACCTGGCACCAAAAAAGAATGCAAAATGTCTCAACAAATGTT

ATATGTATTGCATTTGAGTGATAATAATTGAATATTAGGTTAAATAA
 AATATATTGAAAAATTAACTCACCTATTCTTCCATTTTGTAAACA
 TAGGTACAAAAAAAATTAAAATTACCTATGTGGCTCATGTAGGTGGCTC
 ACATTATACTTGTGACACTATAACAGGCTGGTAGCCATATCTCTTAG
 ACTAGTCTAAGTGTAAACAGTGGTCCAGAAAGATCCAGGTTAACAC
 CAATGAAAGGGCCAGCTGGCTAGCCCAGCTGTGTGGAAATGTTGGGG
 AGTGGTTAAGACAGGGAAAAGCAAAACTTTGTGCTATTGACTTTTG
 AAAATCTTTGTGGCTAAAAACCAAAACATTATT

>Contig49

GCTCGAGTGTGTCTCTAAAGCCTTCCCCATTGGCTCCACTATACGCAC
 TCTCCTGGTTCCCTCCCTCTAGCCGCTGTCTGGTCTCCTTGATT
 TTGCTCGTCCTCTGTCCCCCTGAATGATTGCTCTCCACTACGGGGTGT
 TTTGCTCCCCAGGGACATTGGCAATATCTGGAGAGGTCTATGGTTGTG
 TTTGAGGTGTGCTACTGCCATCTAGTGGGAGAGGCTAAAGATGCTGT
 TAATGCCCAGGACAGTCCCCATAACACAGAAATTTCAGCTAAATATC
 CATGGTCCAAGATCAAGAAACCTGCTCAAATATTAGCATGTGCTGAAG
 GCCCTTCTCTTCTTAGCAATATCTGCCCTTAGGGATCTTTCTAG
 TCTCAGTGGTTAACATTAAATCCAAATTAGCAATAAATTGGGCC
 CAAACTCGTTAGTATAAAATGTAAGTGTGTTATTAGAAGGCTAATAA
 AATGACCTGGTGAGCATCTGCAGCTAGCCTCTGAGCAATTCTGGGACCA
 CGTGCAGATAATCCATCTGTTCCCTCTGTAAATGTGGCGTACCTTG
 TGGCCGATTTTCTCGGGTAAATATCTCTGGGATGCAACTTGTGCGT
 GTTAATGGCTGTGAGGCCAGCGCGTGTGATAAAGGAATCAATCAAGA
 CAATATTGAATTAGAAAGGCAGATTATTAGAGAAAAGGAGAGATACG
 TTGCAAGGGAGCAATGGCAATACAGCAGAGGGAGGCTGTGCAAAGA
 GGCAAGGGCTACGTATGACGTAGGGCTGCTTAGGCTGAATGCTTGAGAC
 AAGATGCTTGCCTGAGGTGGCTGTGAGCTGAGTGCTTGGGTGCTAGTG
 AGCCATTGGCAGCTGACCCCTATTCTTGGAACATTGCTCCCTGCAAGCA
 TTTTAATGTTAACCGCAGGTCAAGTTGAATTTCCTTTCTTTT
 TTTTTTTTTGCTTCTAGTAGGACCTGCCGTTGTGAGACTATCTGAGG
 TAAATTAGACACCCTCTGGTTAACCTCTAGGAGGCTTGTGAGCTAGGCAGG
 GAGCTCTCTTGAGAGGGTGTGGCAGTGGTACTTGTGATGTTGTCC
 ACACCAAGGCAGCTGCTGCTCAGGGCTTGTCAATTGCTCTTCTTG
 CCCAAATGCACTTCTCACTGTTACATGATTTCCTCCCTCTTCT
 TTTTAGCTTGTCTAAATATCACCTCTAGGGAGGCCTCCACACCAC
 CTCTCAAGATTGAGGGTATGCAACCCCAACCCCTAGCCTTCTTATCCCT
 CTCCACTGCTTCTCTCAAAGCACTTGTACGTTCAAATAAAAGATT
 AGTTACTTTATAGTTCTAATTAACTATTTCCTTGTGTTACTTCATCAATAC
 CCATGTAATCTCTGAAAGGAACGTTCTTTGTAGTGTTACTCTAGCAC
 CTAGAACAGTACTTGGCACATGGCAGGTGTCAAAGATTGTTGATTA
 TTTCTCAAAGGGCATGGAGTCTAGAAGTTGAGAACACAGTTCTAAGC
 ACAGCTGTTAGAGACTATGGATGATGCTAATGGCTGTATTCCAGTAGG
 TGGGCAATTCTCAAATTGACCTGGAATCCTTGAGATCTGGGACAGTC
 CCAAGCACTGGCTCTGTTGGGAGAGATGTGCTGGTTAGAGAGGAGA
 ATAGCATCTGGGGACTTGGCCCCAGGGCTTCTGCTCCAAATCTCTC
 CCAACTGAGTCCCAGAGGCAGGAGGCTTGTCTGAGCTGGTCAGTC
 TAACTGTTCCCTCCCCTACACAGATGCAAAGAAGGCTGAGAAAAGCA
 AGCTGTAGGTGAGCAGGGCCCTGACTCTCCCCAGAAGGCACTCAGAA
 CTTCCATAGGCAACTGAAAGAAGGTTCTACTTCCCTCACGGCAGCTGT
 TGCTGGGAAAAAACAGCCTCAGGCCCTACCCCTGTGCTGAGAACCTGAA
 TCCAGTATCAGGTTCTCAAACAAACTTGGATCCAGCTGACCCCTACAAGG
 GGTAGATGCAACCTTGTAGCATATGAAATGGCAGCAAGGTCTTGTG
 TGGACTATGCCCTAGAATCTAAATTAAAGACAAGGCCTCAGAGGGCTAAGT
 GACATCTGCTCCAAAGTTACAGCTAGTGTGTGACTAAATCTGATTC
 CACCCCTCTCAGGTTTACCATATGCCAAAGGTTGAAACAAGAAAAG
 TTATCTTGGCAATTACCTCTTGTGCTTACCTACTAATGT
 TCTAGGCTCACCCCTCTGGTCTGCAATCTCACTGAACTGACAGATCCCTCA
 TGGCCTAAAGGGTTTACACTGGGTTGACTAGGCTCTCCATTGCTGT
 CCTACTGTCTAAGGCACCTCTGGTAGGGTGGCCAGCGTCATTCTGATG
 CTGCTGACTTTCTTCCAGCTACTTGTAAACTTGGTATCCATGGCAGA

GGCTTAAAGGCATGTTCTAGGTACTTTATTCCAAATTCCCCAGTGGC
 ATCAAGGAAATCAGCATCTCTGGATAGCTCTACTAAGGCTTAGTCTCAT
 TGTCCAATCTAGCTCCTGGGTATGGGAGGCATTAGGAAATATTGAGT
 GTAAGAGTGAGTTGTTACCTCCAGAAATATCCTTCAATGGCTCTGAAG
 CAGGCTGTGGAGTCCTGCTGGCTGATCACAGTTCACAGGTGGCTCCAAA
 CCTGTGGCTACATCCATCCTTGTCACTGTCACTGCCATTGTCCCACAA
 ATGTCTTTGGCCTAGCCCCCTGGGATAGTAATCAGTCTTACATAGATA
 TAATTTGTGCTTACATCCACAGTAATTCTGAGTGGACCTAAATAAT
 TCCATGTCAAGGCTCACCAAGCCCAGGGTTACAGATGGGTTACCTTCA
 GCCTTGTAAAGGTGCCCGCTTGTAGTGAGACATGGACTCACACAGAGT
 CCACTCCTGCTGTTCTGCTCTGCTGAGGCTCTGCTGCTGCTGCTG
 CTGCTTGCAGAGGCTGCCAGCTGTGGTGCCTGAGGCACCTGTGTCTC
 ACAGCACCAACTGATGGTGGCCACGGTGTAGTTGAAAGGGATGCTTA
 GATGGGAGGCCATGGGAGCTGCTCAGGAGGAAATCCAAGTCACAGAG
 ATCGAGTCACCGAGAGCATAGTAAACTCAAATCCCTCTGCTTAAT
 AACTGAGATGCTGTCAGTGGTTAACCTCACCAAGCCTTGTTFGTCTC
 ACTTAGAGTGAATTCTGCTTACAAGGCTCCTCATATCCTCTGGGAAG
 GCTCTAGTGTAGTCCACAGATAGCTGGACCAGGCATGTCAGAAATAATC
 TGATTCTCACATTGAGTTAGCCAGCGTCCAGCTATATCCCCATTG
 TGTCTATATAAGTTACCAAGCCCACAAGGATATTAGGTGGCTCTTAGT
 TTGCTTATGATTATGCCCTGTGTGTGTGAGTGTGTACGCC
 ATGAGGATTCCCTCTCCCGTTCTGCTATGGCTCTTCCCCACTGA
 TGGCTGTAGTCCCTGTCCTTGTACTTGGCTTAGTCATGTGACTTT
 TTTGCCAAGGAATGTGGGAGAAGTAACTGGGAGGCCAGTCCAAAGCTAA
 GCCCTGGGAAGCATGGTGGCTATGCCAGCTCCCTCAGAACTCCTCC
 CTTGCCATGAAGAGAGAATAACCTGGATTGTACCTTCAGGCCATGTCT
 AGAATACAAACATGGAGAATAATGAACCTGACTCAAAGGCTGAAGGGCAG
 CTGAGCCCACATGAGGTCAATTGAACCTGAGCTACCTACAGACCTGAAAG
 TGAATAAAACATGTATAAGTCTGACGTTGGGTTGTTACATAGCA
 TTATTGTAGCAGAAACTTAAATAACTGGGGCTAAATATAGTGGACCA
 GTGACAGCACAGAAATGGAAAATGGAGTGATTGTTACTTACATCACAAACC
 CTTCATCTCTGTTGATGGACACTAAATCAAAGTGGCAATTACTCAGAGT
 TGGGAGTCATTGAGTTGACATTTGTTAGAATCATTGACAGTTGA
 GCTCTAAGTGTAGTCAAGAGATGGTTCTCAGCTACAGGTAATAACAA
 AGGCACAGAGAAGTAAGTGACTTCTAGAGGGCTTATTGATATTAGCA
 GCAGAATCAGAGCTAACAAATGAGTCTCTCATCTCCAGCCTTCTATTCT
 TGTTCTAGGGTGGGATTGGAAATAGTGCAGAGAGATTAGCAGTAG
 TGACATGGAACAATGTGAGCCTCAGCTTCCATCCCTGAGGCTGCCTTCAT
 CTGCCAGGGAAATGTCTCTGTCAGCCTGCCCTCTGCACACAGTGTG
 TATGCCACCTGAATAAGTGTCTTACAGCAGTAATGGATTGAAATG
 SGTGCTAGAGCAGTGTCTTAAACTCCATGTATTAAATCATCTAGGGT
 CTTACCAAAACGCATGCAGATTCTGATTCACTAGGTCTGGAGTGGGCT
 TGACATTCTGCACTTGTAAACACATGGACCAACTTGTAGTAGCAATGTAT
 TAGATCATTCCAGTGGAAACATGTATGAGTGATGGAATGAACAGATAAA
 TTAATCCAGGTCTGGTAAGTGAGGTACTGATACATATAAGTTGAAGTGA
 ATTTCACATCAAAATAATGGTACACAGTGAACCTTACTGCCCCAAAT
 CCTTCTTTGAGTGGTTCAAAGTGAACCTGAGCCAGGCCAGGTTAAGTC
 CCTGGTTAGTGTGTGATTAGAAGATTGATCCAGCTTCTCCTCCTTCT
 AATTCTTAAATATGCAATGCCCTCTAGAAACTTGTCTCTCAGGCTCC
 CATGAGCCACCTGTCTTAAATATCTCCCCCCCAGGACATTCTGGGTCA
 AGGAAGGAATCAGGGACTAGGAAAGTAGAAAGGTTGCCGTACAGTGAGA
 AACCTTTGCACTCCTATTGTTCAATTCTAAATGTGGGTATTGTTGG
 GCTCTAATTGGAATCTAACCTGAAATTCAAGGCATGTCAGCTATATAG
 ACCAAGAATTAGGATGAGTTCACTAGAAGCCTATTTTCAGGAGAGCGGTC
 AGTTAAATTGAAGTTATGGGTTATGGTAATGGGTTGGGAGTTACTT
 CATTAGCAATAGCAACGTTTGTGAATCAGAGAAGTGATTTGAACACACT
 GTACATAGTTCTCACTTAGATTATCTCTGGGTCAACCTGTTGGAC
 CTATATTAGAATCATTAGTGAAGAAAAGGTGGGTGTCATTAGGAAAAGA
 GCCATTATTCAAATGTTCTGTTGACATTAGGGCACTGGCAAGACTACA
 GAATCAATAGATATTAAAAACAGCCAGGTGCGGTGGCTCACGCCGTAA

FIG. 4 (34 of 61)

88/18

TCCCAGCGTATTGGC . . TACTTTGGGAGGCTGAAGCGGGTGGATTC ..
 TGAGCTCAGGAATTCAAGACCAGCCTGGTCAACACCGTGAAACCCCTATCT
 CTACTAAAATACAAAAAATTAGCCGGCATGGTGGCAGGCGCCTATAATC
 CCAGCTACTTGGGAGGCTGAGGCAGGAGAACGCTTGAACCCAGGAGGCG
 GATGTTGTATGAGCTGAGATCGCCATTGCACTCAAGCCAGGGCAAGA
 ATAACAAGACTCTGTCACAACAAACAAGCGAACATACGAAACAAACGT
 AACATCCAAACTAGCAGGTACATGCCGTGCAGTCATGACCCATGGTCAT
 AAAGATGTCTACAGCTCAGGAAGCAGCTGCACAATGCCTGCATAGACAAAC
 TCTTATGAAAGCAGAACATGTCCTGATGTCTCATACACATAACAGTGTAT
 GCTTTATTATGGTCATACTCTAGCTGTGATGTACCTACGCTCTAATATG
 CCAACGATAGTTTCTTAAATCATCAACATAATAATGTCATGCTGTCA
 GTCCCCCACATGTAGACATAACTTAGCTGGTACATGGATAAGAAACCTAT
 ATTAGATAACCTTAGGCCAGGTGTGGTGGCTCATGCCTGTAATCCAGCA
 CTTGGGAGGCCGAAGGGTGGATCACGAGGTCAAGGAGATCGAGACCA
 CCCTGGCTAACACAGTGAACACCCCGTCTACTAAAAATACAAAAAAA
 TTAACCGGGCATGGTGGCAGGCACCTGTGGTCCAGCTACTCAGGAAGCT
 GAGGGGGAGAACGGCGTAACCCAGGAGGGGGAGGTGAGTAAGCCGA
 GATCACACCACGTGACTCCAGCCTGGGGACAGAGCGCAAGATTGCTCT
 CCCAACCCAAAANCNANNNAATTGACCCAAATCTGACTAATTCCA
 GAGCCAATTCCAATTAGAACATGTTATATCTCCCTGGTGAACGTGAAAGCTT
 TTATCTTAAGGAGACACACTCTTATGTCACCAATGCTTATTGCTTAA
 AAGTCCACTTGTCAAGATAACAGCTGCTTCTTTAATTAGTTTGTGTG
 GTATATCTCTTCCATCCTTTCTTCAGCCTCTCCATTCTTACATT
 TAGATATATTCTTTCTTTCTTTGAGAGAGAGTCTCACTCTC
 GCCCAGGCTGGAGTAGTGCATGGCGCATTTAGCTCACTGCAACCTCC
 ACCTCTGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCAAAGTAGCTGGG
 ATTACAGGGAGCCCACCAAGCCAGCTAATTGTTGTTATTAGAAG
 AGATGAGGTTGCCATGTTGGCAGGCTGGTCTCGAACCTGACCTCA
 GGTGATCCACCCACCTCGGCTTCCAAAGTGGTATTACAGGCGCA
 GCCACCATGCCAGCTGATTTAGCTGATCTCAAAACAGCATGGGTC
 TGTTGCTTCCATTCTAGCTTATAATGTAATCATTTACATCAAACA
 TCTAATACACCATGGACTGAAACACAGCCATATTGATGAAATT
 AAAACACACCACCAATTAGTCTGAGACACACACCTAACAAATAT
 CTCTGTGATGTGCAATAATCAATCACATCAGTTCTGCACCTCAAAT
 TTCTTCCCTCAATTCTCAGAGATATGGCAATTCTCTGGTTTACATTCC
 CAGAAGCAAAGAAAAGTACACAGCTTCTCAAGTCATGAGTAGCTTCTT
 TTTTATAGCTTGGTGTGCAAAAAGATTGGAATTGCTTACTAATA
 CTAATTTCTGCTGCTGCTGTTCTATGACAAGTCAGAGGGCATCT
 TTTTGAAGACATTCTAAACAGCAATTAAACTCAAAACATGTAATGACAAT
 GACACACAAACTCAACTGATGACCAATGAAGAGTCCAGCCAGTTGA
 CACAAGCTGGCTGACAGAGCTGTAATACACACAGCTGGCATATGCC
 GCCATTCTCAGAGATGTAAGGAAATAATGTTTCCCTAAATCAAT
 GAAATAGAGCATTGGACTGAAAATCTACGACAGTTAGTGTGTTCTAT
 TCATTATTCTCATTCTGTTCTTCTCCCCCTGCTTCTTTAGTTGAA
 TATTCTCTATCTTCAATTCTCTTACTAGTTGAAACTTATGCTT
 TATTCTCTATTCTTCTGACTTACCTAAATTACTCTGTAATCCATGGAT
 CCTTAATTCTTAAAGGCCCCAGAACACCTTCACTTACCTCAATCTCTCC
 CATCTAATTAAAGGCCCCAGAACACCTTCACTTACCTCAATCTCTCC
 AACTTACATGTTTAATGTCATATGTTAACCGTAACTTTAAAA
 CTTCTAAAGCATTATTCTGCTTCTGCTTCTTCTTCTATTGACT
 CATATATTAGAATTCTTCTTCTGCTTCTGCTTCTTCTATTGACT
 CCCCTCTGGGATCATTTCTCTACTGAGTACATAGTTAGAAACTGC
 ACTATTCAATACAGTAGCCACTAGCCATGTTAGCTATTGAAGTTAAC
 TAAGTAAAGTGAATATTAAAAACTCAGTCTCTCATCTCACTAGCC
 ACATTCAAGTGCTCAGCAGCCACATGTGACTAATGACTACTGTACAGCA
 AACATATAGAACATTCCATCATGGCAAAGAGCTCTATTGATAGTGTCA
 TCCAGAGTTCTGTTCCAGGACCAACTGAGGGTGGCTGCTATTCTC
 ATGGCCCAATAACAAAGATGCAGATGAGCTGGGAGGAAGAGAGTTTAT
 TTCTGCAACCAGTTACAGGGAGAACGGCTGGAAATCATCACCAGGCCAAC
 TCAAAATTATGACGTTTCCAGAGCTTATACCTCTAACGCTATATGTC

FIG. 4 (35 of 61)

89/118

TACGTGTAAGTGTGCATI CACCTGAAGACGTAAGTGATTAACCTCTTTIA
 ATCTGTAACTAAGGTCTGAGTCGGAAAGATCTCCCTGGAGCCTCAGTA
 AATTACTTAATCTAAATGGGTCCAGGTGCTGGGTAATTACCCCTATCT
 TGTCCTGCTAAATCATGGAGGTTGGGAATTCCCTTAGAGCACCAT
 TAACCTGTTGTTGAAGGCCCTGGAAATTCTCCAACCCCCATTAAACC
 TGTAAATCCCAAATTGGTCCGTTAAAATTCCCTCCTTAATTGTCCA
 ATTAAAGGCCAAAAAAGGCTGGGCAAACCTCTGAATGGCCTTGTT
 ACATTCAACCTTGTAAAACACCGTTTAATATTAACTTAACC
 ATTAAATCTCTACTGAAACACTTGTATATAATCTGATTAATGAGAAC
 TGGCCTGCGCCATATCTCTCTCAGAATATCTAGGGTTGTGATCCCCT
 GTGTGAAGAGAAATATCTCTGGAGATCTCAATCTCACCCCCAAAAAA
 AATCTCACTCGGAGAAAACCTCAGACTCTTATCTCACAGCGCTATCTC
 TCCTCTCC

>Contig50

GCTTGCTAAGATGGTCTCCTTGTGCTGCCTGCTTCATCCTGGGA
 TCTCCCTCACCATCAGGATTGCCTCACCTCATTCCAGTCCTGGATCTT
 TCTTCTTGTCTTGAGTATTTTTTTTGCTGCATTCCCTCA
 GTGGCCTCTGGGAAAAGATGTGAGGGAGAAAATTCTTAGAAACT
 TGCAATATCTGACAATATTTATCCTATCTGACATTGGTAGATAGTTC
 AGCTGGGTACAGAATTCTAATTAAATTCTCTCTGATTATAAGACATT
 GCTCATTCTCTGGCTTCCAATTGCTGCTGAGAAGTCTGACACCCA
 TTCAAATGCCTGATTTTCCATGTGATTGTTCTGCTGGAGTGT
 TGTAGGATTGCCTCTTATCTACAGTGTCTGAAATTTCATGACGGTAGGT
 CTTCTTCAATTGTTAGACACTCAGTGGGCCATTAAATGGGAAA
 AACATGTGTTCTCAAGTCTACAAACTTAAATTACTTCTCTTCTG
 TCTTCTCTGGCTGTTTCAGCCCCGAGTCCTTAGATCTGCTCTCAA
 TATTCTATTGACTTACTTCATTCTAAGTCTTATCCTTCTGTTA
 CTTCCGAGAGACCTGCTAACCTATCTCCAACCTTTATTGAATT
 CATTTCTTTACTATATAATTAAACTTTGAATACACCTCTCTCCTC
 ACATTTCACCATAGTATTTGCTTCAATTGACAGTCTACTATCTTA
 TTACTCTGGAGATATTAAATAGTTAAATTAAATTATTATTATT
 TTCAAAACAGTGTCTTACTCTGTCACTCAGGCTGGAGTGCAGTGGGTGA
 TCATGGATCACTGCAGCCTTGATCTTGAGCTCAAGCTATCCTCTGTT
 CAGCCTCCAAAGTAGCTGGAACCACAGGCATGTGTCACCATACCAGCTA
 ATTGTTGTTGGAGGTGGAGTCTCACTCTGAGCCGGTCTGGAGTG
 CAGTGGTGCAATCTGGCTCACAGCAACCTCTGCCCTGGTCTGGTT
 CAAGCAATTCTCCTGCCTCAGCCTCTGAGTAGCTGGATTACAGAAACA
 CACTACCATGCCAGCTAATTGTTGATTGAGAGACAGGTTTCA
 ATGTTGGGAGCCTGGGCTGAACTCCTGACTTGTGATCTGCCACTTGG
 GCTCCCCAAAGTGTGGATTACAGGCTGAGCCACTGCACCCGCCACT
 AATTAAATTGTTAATAAGACGAGGTCTGCTATGTTGCCAGTATG
 GTCTGAACTCGTGGCTTAAGTAATCTCTGCTCAGCCTCCAAAGTG
 TTGGGATTACAGGTGTGAGCCACTGAAATCTGACATTAAAGTTTC
 TTCTCTTACCAAGTCTTCTCCCTTCTGTTGGTTGTTA
 TTTGATCTCATCTGCTAGAAACTTCTGAGACGTTAGTAATACTA
 GATTGAGAGTGGCAACTGGAAAGCTGATTGAAACTCTGAATACAT
 GGGTAGGGCTTGGCTGTGAGTGTCTGTTGATGTCCTGGCAAGGC
 CAATGGGTTGGGACCCACTATTAGTATAGGCTGATTCCCTGGAAA
 GGCTCTTGATCTCCTGCCTGGAGGATAAAGGCCTGGCTACAGCCTC
 TGTGTGTAATGTGAGGGAGAAGGGCTGGAGTATTCAACATCATGCTGAAT
 CCTTCAATGATCATCTGTTTAGTAATCTCTACCTTAACCTCTGT
 CTTCTGCTAGTATGGAAAGATGACCTGAAATCTAACCATTTTTTC
 CCCCATTAATCATTTATGATTATTGAGAAGTTAAATAATTGTCATGC
 TGTCTCCAAAAGACTGAATCAACTAGCAACAAATAAGAATTCTC
 AGCTCTGCCAGCATTTAAAAGAATAGCTTATTGAGGCCAGGAGGTCAA
 GGCTGCAGTGAGCTGTGATTACACCACTCTACCCCCAGCCTGGGTGACAGA
 GCAAAACCCCTGCTCAAAAAGAAATTAAAGGAACAGCTTATTGTTGA
 AAATAGACATACAATAAACAGAGCACATATTAAATTGTGCAACTTATAC
 TTGATATAACCCCTGTGAAAACATCACCACAAATCAAGATAGTGAATATAT
 TTATCACCTCTGATACAGTTAGCTCTGTCCTCACCTAACGCTCATG

TTGAATTGTAATCCCCAATGCTGGGGAGGGCCTTGTGGAGGTGAT¹G
 AATTGTGGGGTGCACTCCCCCTGCTGTTCTGAGATACTGAATGAGC
 TCTCATGAGCTCCCTCACTCACTCTTCTGCTGCCATGTGAGGAT
 GTGCTTGCCTCTTCTGCCATGATGTGTTCTGAGTCCTC
 CCTAACCATGCCTCTGACAGCTGCAGAACACTGTGAGTCAGTTAAATCT
 CTTTCTTCTAAATTACCCAGTCTCAGGTGGCTCTTATAGCAGTGTGA
 AAAGGAACATAATACCTCTAAAGTTACCTCAAGCTCTTAAATTCCCT
 TCTCTCCCTCTTCTCATTGCCAAGCAAACACCACCTGTTCTGTCAC
 TATAGATTAGTTACATTGTGGGTTTTTTTTGAGACAAGGTC
 TCACTCTGTTGCCAGGATGGAGTGCAGTGGTGCATAGCTCATTGC
 AGCCTGAACCTCTAGTTCAAGTGGTCTCCACTTCAGCCTCTGAGT
 ACCTGGGACTACAGGGTACACCAACACAACGGTTAAAAAATTTTA
 AATAAAAATGGGTCTTGTATGTTCTCAGGCTGGTCTGAACCTCTCG
 CCTCAAGCAGCCTCCCTTGGCTCCAAATTGTTGGGATTACAGGC
 ATGAGTCATGACTCCTGGCTAGTTACATTCTAGAGTTGTATAAA
 TGGAAACATACAGAATGTTTTTGCGGAGTGGGGAGTGTCTTCTATT
 TCTTCTTCTTTCTTTTTTTTTGAGACGGAGTCTCG
 CTCTGTCTGTTGCCAGGCTGGAGTGCAGTGGTGCATCTGGCTCACCG
 CAAGCTCCACCTCCGGTTCAAGCAATTCTCTGCCACTGCCCTGAG
 TAGCTGGACTACAGGCCGCCACCACACTGGTAATTTTTGTA
 TTTTGGTAGAGACGGGTTTACCATGTTAGCCAGGATGGTCTCGATCT
 CCTGACCTCGTGTGATCTGCCGCTTGGCCTCCCTAAGTGTGGATTACA
 GGCCTGAGCCACCGTGGCCGGCCAAGTGTCTTCTAAACAGCTT
 TCATGCAATCTTTTATTTACATCTCTGTGATCCCACCTCCAAAGG
 TACTAGATGTCATTGGCTCTAGGATCAGCTACCAATTGCCAACTGCT
 TTCCAGCCTTCAAAAATTTTCTTTCTTAAAGATACTCTGTG
 TGAGGCTCAGAACTCTGAAATTGCTACTGCAAATATGAACTCGGTGATGT
 GAATGCCAGGGATTGCCGATTGATCAAAGAAATGTATCCCCTCTCC
 TCACTCTGCTGCTTCTCATTGTTCCCCATCTGTGGATTGTA
 ATTAAATATCCCTTAATGTTATAATATTAAATGGCTTGGGAAAA
 GTACAGAATTAGGTGCAAGAGTGCATAGCTGTTATTGTTGGCCTC
 TGAGACTGTTCATATATGCAAGTTATTAACAGAAAGTTCTGAGT
 TGAGATGTCAGGGGGTCTGATAGAGTACGTTGAAGGCAGTTACTGGAA
 AAAATAATGCCATTCTGGTTGACTTCGGTAAGTTAGATGCCAA
 TATATTGTTACATGTGGCATTCACTGGTAAAGTAGCTTCCCTCC
 CTTCTCTTCTCCTCTGCTTCTATAAGCATCTGTTGGGAA
 CTTCTAGGAGGAGAGCTGCCAGCCGTGGTAATGGAGAGGTCTGCA
 GAGATAAAAGAGATGCTCCACTCAATGCAGGATGGTGTGGAGGTAAATG
 GGGATACGTCTGGCATCACTCAGGAATGGCCTTCTGGCAGGGAGAGA
 AGGGAGGGAAAGAGGAAGGGAGTCAAAGATGAATTGCTGAATACGGGG
 TTCCAGGGCTGGAGCCAGGAAGAGAACCTTGGGAGGTGTGAACCTGGAG
 GGCATCAGCTGATGAGGAGCAGCCTGAAGTCCGGGAGGACCTGTTTG
 GTGGCCAGGAAGAAAGTGCCTTCCACACACAGGGAGGCCACAAGGCTGAT
 GGGCTGGGGTTGGAAGGACAGCCCTAGGACAGGCTGGGAAGCAGGCTC
 AGGTAGGGACTGCGAGGTCTGAGTCATTCTGGTCTTAG
 AAAATAAGATCCAAGGCCCTTGAGAGTGGAAAGGTGGGAGGAGGG
 CAGATGGGCTTAGGCCAGGACACCGTAGAGCTACTGCCAGCTGTCT
 CTCAGGGACTCTGCTGAGGTCACTCAAGGATCATTCTAGCCTGCTAG
 ACAGTACTGACAGAGGGAAACCGTAGTATCGCACCCACTTCTCTTTC
 AATGAAAGTTAAAGGTACCATTCTCTGGCAAAGGAAGTCCACAAA
 TATTCCATTCCGGCTTAGAAACAGCAAGGTATCAAGCAATTGCAAAC
 TCCTGTGCTGGGAATTCCAAGGAAGTAGGGGAGAGTTCTGGTGGAGA
 CAAAGTGAATTCCGAGTATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCA
 GTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGC
 AGCAGAACAGAACCTCCCGCACGTGTCTCAGGCTCTCATTGCCAACT
 CAGTCTCTAAGTATTGAGGAAAGAATAGCTATGAGTGA
 AATAATTCAATTAGACCTGAGCCTCATCAATTGTTAAAGGCCTGA
 CTCTCTTACCTTCCCTGGGATGGAAGATGCAAATGTTCTGATGTCAC
 TGTCAAAAAGAAGAACAGTGGGATATTGAGTGTGAGTCCAGCCA
 TTTGTCACAATAGATGAGATGACTGCCATGTGTAGACTTTCTATAGA

FIG. 4 (37 of 61)

91/118

CTGTGTGCTAAACCGA C TGCCACTCCAAGGAGTAGATGAGGAATG C
CATGGTCTGGGGAGCCCTACCCCAATTGGGGCAGACATTCAAAGCTC
ATTTCTGTGGAGGGGGTTGATGGTTAAAGGACGGCCTGGAGTAACCG
TCTGTACTAGGGCCCAGGAGAGTTACATGCTGCTCCATGTTATTCA
ATTCCCCATGTGAATAGCTATGGCGTGAGGTCCAAGGTTAGGCCTTC
TACCATAAATGGGGAATAAAATTCCCTACCAGCCTGAGAAGTTCTGT
TATAAGAGGCTTTTTTGCGGGGTGGGGAGCAAGCGACTAATGT
GTTATTCCATACGGTTGTTAAAATGTAGATGTCATATGCAGGAGAG
GTGGTGTAGTGAGTCACACGGGATTAGAAGGACCAGTCGAAAAGCAGA
AGAGGGTCAAGTCAGGGCACTGAGGACTACTGCATTCACTGGCGTAAA
GGCAGATGGCTGAACAGGAGGGGACATTACATTGCTTCTCCTTGAG
CCTGATTCTCATCTAAAAGAGGGTCATTATTACAGAACATTAT
TAAACCTGTGCCAGGCACCGTGCAGGAGCTGGACTAAAATTAATCCA
CCCCTGTGAGCTGCTGAAGGCTAAAATGAAGTATGTTAAAGTAACC
AAGTGTGTACACATGCAGCTATTCAATGACTGTGTGGCATTGCGGCAG
ATTTAATTCTTTTATTCTCTCTTAGTGAGAGGEGTTGGTGT
TTATTATTGTGCGCTGTAACTGCTATTCACTTGCTTTTTGTTGCC
TCCAGCCCATTCCAGGGCTGTCTAAGACACTTCTTATCACCTAAATA
ACCGGGGAGGCAAAGCGCTTCTTAAGAGATGGATCCAGAAGAACATGC
TGGTTTCTGTAGAAAAAGGGGCTGTGGGAAGTAGAGATAAGAAGGGAAAT
TGGCCAAGATGAATGTACAGAGCTTATTTTTTATAACACAGCAAG
ATTAGATACAAAACAGGACAATAGCATCATCTGTTTATAACTGGAAAG
GACCTCACTTACAGGTGGGGAAAGAATAGAGTGGAGAAGTGAAGAGAATG
GTCACAGACTCAATCAGCATGTCTGCGTCAAAGCTGGATTCCAATTCA
GGGCTCTTACAGTGACGTATGGCTAATATTTGGCATTGTTGGGG
AAAAGCTGAAGCCCTGATGGTGTACGTCACTCTTGAGATAGTCTGTAGTC
CAGCAGGGAGGAAAGCAAGGAAGGGAGGTGGAGGCAGCATTGGGGTGT
AACATTGCTCTTGTGTTGTGGCAAATCATAGTGTGATTGGACAAGC
CACTGCCCTCTGTGAGCCTCCACTTCTTCTTAAGAGGGAGGG
AATAGTAGAGTAAAGTAGTCATTATCAAACACCTGCTATTGGAGC
CATATTGCAAGTGGTTGGGGTTGAACACTTGGCTTATTACCCATAGG
ATTAAATCCAACCTCGATACTGTGGCATTCCAAACTCCAGTCTAATCTT
CTTCTCATGCCATGCCACACCCCTGGCATATCTGATGTTGCC
CCTGCACTTGCCCCCTCCTTATCTTGCTTCTGACCTACCATATGGCT
ATTGGTTGAAATTCTCATTTCCAGGGCCTGCTTAAATATCATCTCATC
CATAAAACCTTCTTGTGACCTCCCTTGCCCTGTTCTCCATATGTCTC
AAGCCAGAATTATTCCCTTGCGCAAGGACTGGTTTGACCTC
TCTCACGAGACTTAATATTGAGACCAAACGTCTTAGACCTCACCAGCCA
GAGAGATGAGCATCTATGGAATGCAGGCTTGCCTGGACTTGTGATGC
AGGGCCTCTGCCCTCCAGGGCTCTCTGCTGTTAGGAATTCCC
TCATGGCACAGTCATGAGCTAGGGCTAAGTCATACATGTTTACTT
CTTCTACTCTGCAAATGGTCTTCTGAACTCTGAGGGCTCTAAAGCTGCT
CTGAGTTGTGGGTGAGTAGAAAGGGCTTCAAAGTTGTGCTGTTG
TTTCCACCCCAATAGCATGAAACACAAAGATGCTTACAAATAGCTGCT
TGCTTCTAGCCCAACTCTCTCTGAGGCTTAAAACAAGTCCCCT
AGGTGAGCTGGACTGGAGTTGATCCTATCTCATTATCTGCTACTCT
CTTCTGCTCTAGAGAAGATATTATATATGTGTGATGTGATGTGAAA
TATATAATATCCATATAGAACATATATTGTTATTTACATATACATA
CATAACATATGCATGTATTCAATATACATATGTAGTATCAAAGTTGGAA
TTAAACTGTATATTGTAATTGCTTTATTGCACTATCAGTAAAGTAAA
ATGAATATTATCCATACCGTAAGATATTCTCAATGTTATTTTTTT
TTGAAACAGGGCTTGCTTGTGCCAGGCTGGAGTCATGACCCGA
TCTGGGTCACTGCAGCCTGACCTCCCCGGCTCAAGTGTATCTCCACC
TTAGCCCTCTGAGTAGCTGGACTAAAGGTGTGCGCTCCACACCCAGCT
TTTAATTCTTGATTTTTAAAGACAGGGTTTGCCACATTG
CCCAAGCTGGCTTGAGCTCTGGTCCAAGCAATCTCCACCTGGCC
TCCCAAGTGCTAAGATTACAAGCATGAGCCACCACACCTGGCTCAATG
TAATTGAAATGGCTGTAGTATTCCATATGTGGTTGACCCAAAATT
ATTAACCACTGCCCCAGTTATTCAATTTTTTACTATTGAAATAA
TGTGTTAGTAAATACCCACAAATATGTACAATGGCTGGCTTAGTGGCT

CACCCCTGTAATCCAAACTTTGGGAGTCTGAGGCAGGTGGGTACACCTG
 AGGTCAAGGAGTCGAGACCATCTGGTTAACATGGTGAACACCCCGTCTCT
 ACCAAAAAATACAAAATTAGCCGGGTGGTGGCACACACCTGTAATCGC
 AGCTACTTGGGAGGCTGAAGTAGGAAAATCACTTGAAACCTAGGAGGCGGA
 GGTTGCAGTGAGCCGAGATCACACTACTGTACTCCAGCATGGGCAACAGT
 GAGACTCCATCTCAAAAAAAAAAAAAAAAGTACAATTGTTG
 TACCTCCCTGATTATTTCTTTAAGTAGAATTCTTATAATTTTTTA
 TAAGTAAAATTGAACTCAAGGGAGAACGCACCTGGAGTCCTCAGATACC
 TATTGCCAAACTGAACCTTCTGTTCCAGGTTACTACATTAGCCTGAC
 TCAGGGTTGGGGAGTAGAGGGAGGGGGTGGAGGCAGAGGGCCTCTCCCTG
 TCCCCACAGACCTCCCTGGTGAGGTCCAAGTCTGGACAGGTGGAGTGTG
 GCATTGCACCGTCAGGTCTGCTTCTGTAATTCCCTAAATCCATCCAG
 TGGAGCCTCATGTTCAAGTCTTTTTTTTTTTTTAACTCCC
 CTGAAGACGGAGTCTCACTCTGTCGCCAGGCTGGAGTCAGTGGCACGA
 TCTTGACTCATTCAACCTCTGCCCTCCAGGTTCAAGTAATTCTCCTGCC
 TCAGGCTCTGAGTAGCTGGCACTACAGGCGTGTACCATCACGCCGGCT
 AATTTTTTTTGTATTTTAGTAGAGACGGGTTTACCATGTTGGCCAG
 GCTGGTCTCGAACCTCTAACCTGTGATCTACCCGCCCTGCCCTCCAAA
 GTGCTGGGCTTACAGGTGTGAGCCACCAGGCCCTGCCCTCAAGTCTATT
 TTAACCTCCAGGAGGCCTGGTATTAGGGATTAGGGCTGGCAGAAGGGC
 CTCAAAGCTTCAAGGCCCTGGGAATAGGCTGCAGGCCCTGGTCAGGGTAA
 CCCAAGTGATTGGTCCAAAGGGACAGGAAAAAAAGTGAATTGATATGG
 AAGTGTCAAAGTGCACACTGTCAAGACATTAAAAAATGTAACCCCTTTAC
 TAATATACAGTAGACTTGTAAATATTAACTGATTGAAAGGAAAAA
 AACCAAGACGCAGTTTCCCTACCATACTGTCAACACCTCAACACTGAG
 TTCTCTGTGACCTCTAGTCACCGAAATGCTTGGGATTCTCCTCCACAC
 TAGTCTCTCCAGCAGCCACACCAGTTGGGTGCTCTAACTCACTCCAAACAC
 TATCTACCTGGAGTTAGCGTTAGATCCCACAGGTGAGGGCTCAGTCTCA
 CAAGACTGCCCTCCACTCAGGTGCCAGTTACAAGTGGTAGGTTGTCAAC
 TATGCTCTGACTGATGGCTATAAAATCTGGGTTGCTTCCCTGGGTTCC
 GTGAATTGCTAGAGCAGCTCACAGAAACTCAGGAAACACTTAAGTTAC
 CAGTTATTCTAAAAGATATTACAAAGGATACAGATGAAACACCAGATGAA
 GAGATGCGCAGAGCAAAGCATGTGAGAAGGGGTGTGGAGCTTCATGCC
 CTCTGGGGCACCCCTCCAGGAACCTTCATGTGTCAGCTATCTGGGAG
 CCCTCCAAAACCTGTCCTTTGGGTTTAAGAGTGGCTTATTACAT
 ACACATGATTGACCGAACATTGCCATTGGTACTGACACAAACCTTCAG
 CCCCTCACTCCCTCCAGTGGTGGGAGTGGGCTAACAGTCTCAAGTC
 TCCAATCCTGCCCTGGCTTCCCTGTGACAAACCCCATCATGAAGCTACT
 GCATTGGGCTGCCAGCCAGCAGTCATCTATTAGCATGAAAAGACACTC
 TTATTATTCCAGAGATTCCAAGGGTTTAAAGCTGTATGTCAAGGAAAC
 AGGAGATGAAGAACAAATATATTACACATCACACTCGTGGGGAA
 ATTGACAGGATAGCAAACACTGATTAAAGGAGGATAGGAGAGACTGAGATA
 TATATTCCATATATATATAGAGAGAGAGAGATATTCCATATATA
 TATATAGATCTAGAGAGAGAGAGATAGAGAGAGAGAGAGAGTCTTCC

>Contig51

ACACATTGGGGAGCAGTTCCGGAGGTACAGCCGGACAGGAGATGTGA
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 CCTCTCTGAGGGAAACACTTGTATAAGCATTGCAATCAATGGGCTCTT
 TAATTATGTGCCAGTGGCAAGAGCGGGTGTGAACCCAGGGGCTGCC
 AATCCGGGCCTTGAGGCAGAATAAAAGTGGTCTCAGGTTGTTGGCATT
 CCTTGCCCTCCACCCGAAGCAGACACAAACCTCTGGAGGCAAGTTC
 CCCAATTGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAG
 CTCACAGACAAAGGTACCAAACACACAGAGCAATAACAAATTGAG
 TGACGTGAATGAGAATAAAAGAAACAATAACCACAGCTGGGATGCTCT
 AAGTCTTCAGCTGTTAGAATTCTGAAATATAGAATAAAACTGCCACAAATG
 GCAAACATGCATCTAGTACTTACTGTGCTGGGTTCAAGAATTGCA
 CATTGTGCCAGATACCGACTCAGCTTACACTCACCCCTCTACTGTGCC
 TCTTAATTGCACTAGATTAAAGGTAGAAAGGAAGAGGGCAGCTATTCTG
 TTCTGGCTGTGCCCTGGCAGCACATGCAAATGGCAGTAACAGTGGC

AGTCACAGGTAAAGTAGC TTCTCACAGTG GAGAGTTAAAGGCATGGGA
 GAGACGAGCAAGGTTCTAAAGGGACAGTGGCCAGTAATGACCAGGGC
 TACTGGAGTGGCTGCATGGCTCTGTGGAGCTCAGAGGAGCCTGGGTCC
 TGCAGGTGCAGTAGCAGCTTCTGTAGTCTCTGATCTCTGGGTCCCACAA
 TCTTCCCCGTTTGTCTCCACTTCTAATTGTAACTGACTTCCCTG
 TGTGTACTTCTCTCTGATTGAAATAGCCAGACTGGTTCTGTTCTG
 ATAAGACATTGCTGGTACGAACACAGTAACCTATTAACTCGATATCTC
 TATGAAGGAGGTACAATAATTATTCTATTACAGATGAGGAACACAG
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 GTTGATATAACATAAATTATTAGAAAATCTAAGGAAATAAAGGCA
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 GTAAAAAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTTAAATA
 GCTGAAGAAATGATTAACTGAACTGGAAGGTAGTCTGAGGAAATCAGAAT
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 TTTCAAAATAACAAAACTGAGAGAGTTACCAACAAAGCATTCTTA
 AATGGACTTTAAATGCAGTTTAGGAAGAAGGAAACAATTCTAAGG
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 CTATTAATAATGAGTTGATAAGGATAAAGAAAAGGACAGAATTAAAATAC
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 GAAGTGGAAAAGAAAAGGTAGAAGAAACAGGTCCAGAAATATCACTGAT
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 TCTAGTGAUTGAGTAGTCAGTCAGTCAGTCAGTCAGTCAGTCAGTCAG
 TTATTGTGAGTCACCTGTGATGATGAAAGGTTAATTCAACAGAAAGAC
 ACAATTATAAACTTGTAACTCAAATAGTTTATTTCATTTCATTTCATT
 TTATTTTTTGAGACAGGATCTTGTCTGTCAGGCTGGAGTGCAG
 TGGCTTGTCTCAGCTCACTGCAGCCTCCACCTCTGAGGCTCAAGCTT
 CTTCTGCCTTAGCCTCATGAGTAGCTGGGCCACAGGCACACACCACCA
 AGCCCTGCTAATTTTGATTTTGAGAGATGGGTTTCAACATGTTA
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 CCCAAAGTGGGATTATAGGCGTGAGCCACGGTGCTGGCTCAAATA
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 CAAACAGACAAAAGACAATGACAAAAGTAAATGCAATGAACACTTTGAT
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 CATGTTCTGTCAGCTCAAATCATCTCTGCTGGAAATAACTACTTCAT
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 TTTTCTACTTCCATTATATTGATCACATCTGTGCCACAGTTTG
 CTTTGTGCTGCTTTACTCTTCTAGACCCCTGAGAGCTCCTGAAGGGT
 TGGGTCTTCTTCTTCTGCTCATTCCTCATGGCACAGTGAAGTGCCT
 AATAATGGCTATTGACTGAAATTAAACTGTATCTAAATGGACATATTCC

FIG. 4 (40 of 61)

94/118

ACTTCTGGGCCATTCAATCTTTCTATTGGAACCAGGAGATGGGGAA
CCATAACAAAGGTAAAGGGTGTGCCATGTGAAAGAACATGGAACCTCCCC
TGAGGGCCAAAAAAGAGCAGGGAAAGGTGCAAAGACAAAATCTTCATTT
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TTACCTTAGTGTAGGGAACTGAGGACAGGAATTGTTGATGCAGACTC
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GTAGGCTTATCAGATATTGGAGATATCTCATAAACGATGGCTTGGTT
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>Contig52

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 GGCCTCTGAAGTGCTGGATTACAGGCTGGCCTCTACGCCGGCCGAG
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 CTAAAAATACAAAATATTAGCCAGGCGTGGTGGCGGGCACCTGAGTCCC
 AGCTACTCGGAGGTGAGGCAAGAGAATGGCGTGAACCCGGAGGCAGA
 GCTTGCAGTGGCAAGATTGCGCCACTGCCCTCCAGCCTGGCGACAGA
 GCGAGACTCCGCTCTAAAAAAAGACTTGAGGGAGTTGTTTATT
 TTGTTTCTTTAAGACAGGGCTTTGTTGGCGCGGTAGCTCACGCC
 TGAGTCCCAGCACTTGGAGGCTGAGGTGGAAAGATCTCTTGAGGCCA
 GGAGTTGAGGCCACTCTGGCAACATAGCAAGACACCGTCTCACAAA
 AATGTGCAGGTTGAGGCTGCACTGAGCAGAAAACACCGCTGCACTCTAG
 CCTGGATGACAGAGCGAGACCTGTCCTGGAAAAAAAGAAAAAGACA
 GGGTCTCGCTGTGTCACACAGGCTGGAAATGCAATGGTCAATCATGGTTC
 ACTACAGCCTGGAACTCTGAGCTCAAGCAATTCTCCTACCTGGCCTAC
 CAAAGTTCTAGGACTACAGGTGTGAGGCCACACGTGGCTCAGGAGAG
 ATCTTAATAATAAAAGGACAAATTGCCCTGTCATCCCTAGGGCAGGATT
 GACACATCCAAGGATCAGGCGAGAAAGCCTGTCGGAGTGGATGAGCAAA
 GAGAAAGGCTGAGAGTTGAGAGGGAGATGCACTGCCAGCTAGGACAG
 GCCTTTGGCTATGGAGGTTTCAGAGGAGACCCACCTAAACTAAC
 CCATAACATTGCACTGGGACCTGTTGAAGTCATGGACTACTACCTGAAA
 GCCAGAGAAATGGGAGGAGCCTTCTGAGGAGGGACTCTAGTCCATA
 GGTATCTGCCACCAAATACATGGACAGGCCCTGGGGAGATGGTGGTA
 GCCCAGCTGGAGGAAACCATTTGCCACCTGAACTAGCCAGGTAAGCC
 ACCCAGGCACTGAGGTGCAACCCATGCATGCACACACAGAACACT
 CCTCCTATTATTCTCAATTCAAGGGTCTAACACCCATTTTTTGTT
 TTTGGGTTTTTACATGTTACATTTATTTATTATTATTGTGA
 CAGGGTCCCACCTGTTGCCAGGCTGGAGCACAGTGCAGTCGTGCAATC
 ATATTAGATTGGTGCAGGAAAGTAAATCACGGTTTGTCAATTAAAGTTTG
 CCATTACTTTAATGATAAAACACGATTACTTTGACGCAACTAAAA
 GCTCACTGCAGCCTCAAAATTCTGGCTCAGGGAAATCCTCTGCCTCAG
 CTTCTGAATAGCTGGACTACAGGCACATGCAATCCACCTGGCTAATT
 TTTAAAAATTGGTAAAGATAGAAAGTCATTTGTTGCCAGGCT
 GGTTCAAACCTCTGTTGCTCCCTCTGCCCTGTGCAAGACCTTC
 TGGATGCCACTAATGAAGACTCCAGGGAGAGGAAAAGTAAACATAGGT
 CCCTGATCAAGGGACCAGGGTTATGACCCACAAACAGCATGCCAGATT
 CCACTGGCAGTCCTAGAGGTGCGATTGCCCAAGTGTGTGGAGGCC
 TCTCCCTAGCAGTGGTTATACACCAGCCACAGCACAGCATATTCTCTT
 AAATTGTGAACATTGCAAAACCTCTGAGGGACAACATATCATGTTGT
 GTACTTTGTTGTTGCCCTCCCTATGACACGCGCGCATGCACT
 CATGCACGCACGCCGCGCACACACACACACACACACACACACAC
 TGCTGGTGTGCTGAATGGATGAATGGCTAATGTAAGTCATTCTAAAAGC
 TACTTTCTTGGCATACCATCACCTTGATTGATTCATTTCTGAACTCCT
 ATGTTCCCAGATGAATTGGAAAGCCCTAGGGAAACATTTCAAAATTGCT
 ATATGGGAGAAATGGGAGGGTCTCTAGAAATTACCTGCCACAGGTAT
 TTCTGGTAAGACACAGCAAAGGTGGCACCCATTCTCGTTACAATGT
 CAATGCCAGTCACCTCTGCCCCATAAAACATTAAAGGTGCAGAAT
 TCCCATGGAAGCAGGTGGACACCATCTGCTCCAGCCAGCCAGGGAGCA

FIG. 4 (45 of 61)

99/118

AGGTGTCCACTGTGCCITTGGCAGGAAC TGC GCTTCTCTACTCTCCC
 CTTGAGGCCTCTGGGCTGGCCTGTCCTCAT TGACAAGGCTGCT
 TACTGAGCAGTT CATTCTGAGCTGGACATAGTGCTTCTGGTGAGTCTCTA
 CTTCTATTAACCAAAGATATTCTTCTAAGGAAACGCTTCCGTGCG
 GGGGAGGTTAGCTCCAGATGGAAGTCACAAGTGATGGCATGGTAGCTCTC
 ATCCGTTGGGATGATATTCA CGGAGCACCACTGAGCCAGTCATG
 GAGGTGAACAGTATATGCCAGCCCTGAATCAGGTGATTGACAGCAAGGG
 AGACAAGCAAACAAAGCTGAGGTTGCTGAGGATGTTCAAGACTCACACA
 GCACAGAGGAGCATCCACCACCCAGCTGGGAAAGGACTTGTATAGAGG
 GGGTGAAGCATGAGCTGAGCTTGAAGACTAGAAATTAGCAAAC TACA
 AGGAGGAGAAGGAGTTCCAGTCAGGAAGAACAGGTATGCAAAGCACA
 GAGACTAGAAAATATCACATTCAAGGAAC TGCAAATAGACAGGAAAGA
 TTGATGCGTGGGATAGGAGAGGGCAGGGGATTCCAGGTGGCCCTGC
 TTGCCCCACTCAGGAGCTTGAACCTTATCCACAAAGGAGGTGTGGAACCA
 TAATGAATGGGTTTGTGCAAGGGCTTCA GTGCA CACAGATTGCTTTTG
 GAGATACTTCTGTGGCTGATATGTGAGGAAGGGATGGAGGAAGTTCCGT
 GGCAATCAGGAAAACCAATTAGCAGATGATCAAATGGCTAGGGAAAAA
 GGGAGGAGGACTTGGACTACCATG CAGCAGCAGAAATGGAGAGAAATAAC
 AGATCCCAGGCACTCAGGAAGCGCTCAGAATGAGCCCTCAAAGAAACTTA
 TGGTAGGTGATGGATGGATGGAGTGTGAGTCTGGGATAGCATTGCTGG
 GAAAATACTTCTAGTTGAGACAGGGAAAGTGGCAGCAGAAATGGAGGG
 CTTCTCTTTGCTTAAATACTTTATAATATTGGAACCTTGAAAAT
 GAGCAGATATATTAGCAAAGCCTAAAGGGATATTGAAATCACTG
 CTAGTTCTAACATATAACCTTCAGCTTGCAACATCATCAATTAACTTTG
 ATAGCCCTTCTGAAACTATCATCCAAATAGCAATCCTTGAAAC
 TATTGAAAACGGGCTTGTAGGATAGCCTCACAGATGTTGTGGTA
 GATTCTAACATCTAATGTCAAGGGAGTGAAGGAATCCCCTAGAAGT
 TGGAAAATTCTGGAATCTCTATTCTATGGTATTAAGTTGCGGTACAC
 AAAAGTTAACACCTTACACAATCAGACTCCTCATTTACATTGCTCG
 GTAATTAGAGGAAATCAGTCACCCAGAGCCTGGGCTAGACTTGACAAA
 ATGCACCCAAACAAATCCTGAGTGGCCTGCTGAGGACTTCTCCAGAAGA
 TAGAAAATCAGTCCAGCCAACAAGGGGAAGCAGCTGAAGAAGTGA
 TTAACAAAGTCTGGAAAGGAATGACCAATCATCTTGATTGTGTAATA
 ACCAGAGAGTAAATACAGTACCGACAGACATTGGGAGAGAACGATT
 TATCATAGCTTTAGAAGAGAATATTTCAGCATCATAAGCACACAATT
 CCAAGACAGAATCTTCAGGGATTGTTGACG

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ATGTTNNGGTTTGGGACCCATTCAAACCTCATGTTGAATTAAATCTT
 CAATGTTGAGCGAGGTCTGTGGGAGGGTGAATTGGATCATGGGGTGGG
 TCTCCCTGCTGTTCTCAATGATAGTGAGTGAGTTCTCACAAGACCTGGT
 TATTGAAAGTGTGAGCACCTCTCCCCTTCACTCTCACTCGTCACTG
 CTCCGCCATAGTAAGATGTGTTCCCTTGCCTTCCGCTCATGATT
 GTAAGTTCTGAAAGCCTCCAGCTATGCTTCTGTACAGCCTGTAGAAC
 TGTGAATCAGTTAGACCTCTTCTTCAATAATTACCCAGTCTCAGGTCA
 TTCTTATAGCAGTGTGAGAGTGGATGAATATAGTGCCTATGTTGTAT
 TCCAGCTACCAGGAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGT
 TTAAGGCTGAGTGA GGCATGACTGTACCACTGCTCTCCAGCCTGGGGA
 CAGCGAGACCTGTTCAAAAAAAAAACCAAACGTGTAAATGTG
 TTCATAAAAGTGTCTGCTCCACACCTGTCCTATATATCTTATTCTC
 AGCCTCCGACAACACTTATTCAATTCTATGTATCTCCAGAATCAA
 AAAAAAAATCAAATACAAGCACAGTGGAAATGATTGCCCTTCTCC
 CCCTTTGTTACATCAGAGTTAGCATATCATAAATACGGTCTGCATTTC
 TTCTTTCTAGCTATCAGCATGTTGGAGAGGATTCTATATTGTGCA
 ACAGCATGTATTAGTCAGTCCTGCATTGCTATAAGGAAATACCTGAGAC
 TGCATAATTATAAAGAAAAGAGGTTAATTGGCTCACAGCTTCGAGGC
 TGTTCCACAGGAAGCATGGCAGCATTGCTTCTGGGAGGCCTAGGAAG
 CTTTACTCATGCAGAAGACAAAGCCGGAGTGGATGTCTTATATGGCAGG
 AGCAGGACTGAGAGAGAGAGAGAGAGAGAAAGGATGCCACATACTTT
 AAACAACCAGATCTGTGGGAACTCTGTCA CGAGAACAGCACCAAAGGGA
 TAGTGCTAAACCAATTCAAGAAC TCCACCCCCATGATCCAATCACCCCA

CACCAAGGCCCCACCTCCAACATCGGGGATTACAATTGACATGAGATTG
 GGCTGGGACACAGAACCAAACAATACCAGAGTGCTTCATCTTTCT
 ATAGCTGCCTAGTATTCTATGTCTTACTTCATTTAGGCAGTCCTTGT
 TGATAGACACTGGGTTACTTCAATTTCCTATTACAAATGATGTGCA
 ATGAATAATTGATCATTTCAATTCACATGGGTTATGTCCATCTGTG
 GGATAAACTCAGGAGTCAAATTGCTGGATCAAAGGGAAAGTGCACCTG
 TGATTTCATAGTTAGCAAATTGTTCTATAAGGGTCATATCAATTAT
 AGTCCACCGCTAATATTAAACAGTGGGATTCCGACAGTTGACCAA
 CAAGGTCTGTTAAACTTTGATTTGTCATCTGATGGGAAAATAC
 TAGTATCTCAAAGTGCCTTAATTGACTTTTCTTACAATGTTAAGCA
 TCATTACTCTGCCAAGATCAAATAGTATTCTTCTGTGAACAGA
 CTGTTAAGATCCCTGCCTTGTGATTTGTTCTTCTTCTGTGAACAGA
 CAAATGTTGAGGAGTCTTACATGTGAAACAAGTTATCTCTTATC
 TGGGGTGTGAGTTACAACACTTTCTCTGGCTTGTGCTTGCCTTGC
 TTGCTTCTGGTGAATTCCGCAATTCTGAAAGTGTACTTTGTCATCATT
 CATTCTTACACCCATGCTCTGTCAGCCTGGTCCCTCTA<CTGAGGG
 CTTTTCTTTCTTCTATCTGGAACATTTTAGAGACAGGGTCTCA
 CTCTGTCATCCACGCTGGAGTGCATGGTGCATCACAGCTCACTGCAGT
 CTTGAACCTCTGGGCTCAAGCAATCCAGTGTCAAGCTCCAAAGTAGC
 TAGGACTACAGGTGCATGCCAGCATGCCAGTGTGATTGTTTATTATT
 ATTATTTTTGAGAGATGGGAGTCTCACTATGTTGCCAGGCTGGTCT
 TGAACCTCTGGGCTCAAGCGATCTTCTGCCCTGCCACCCAAAGTGTG
 GGATTACAGGGCTAAGCACCAGCCCATGTCAGGAGGGACTTGTGAAATCTTGTG
 TTATCCCCTTAGGCTTATGTCGTTCTCCCTCCTCCCTGG
 CTACTCCTCTGTTCTTACTCTACTGTCATGTTACCTTGTTC
 TGCTTATAACTAGCTGCCCTCCTATCTGAGGAGGGACTTGTGACTGTT
 TCATCTGTACTCCAGGTCTAGTACATAGCGCTGCTCAACAGATGT
 TTGGTGCATTGATAGATAAAATCAATGGTAGCTGTTAATACCAGTCTGAC
 TCCCTGCAGTCTCAGCTGATCCCTGTTCCAGATGTGCACTGAATATCTT
 TCTGTTGAACAAACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTCGG
 TGGCCAAGGATATTGAGGTACTTGCAGCACTCAGCAATGAGGAGTGG
 GCTTAGTCCCCAAGAACTCTCACAGCCCTGTTGCTTTACTGTTCA
 TGTCAAATCCAAGACAAGTCAATGATCAGGAAAGACCTTTTTCTTC
 AGTGAAGTTTATTGAGGAACTGAAACAGTATGATATTGCTCATT
 AAATATCCCATTAAATAATCTGAGCTTATATATTTCAGTCTAATT
 AAGGACTTGATTAAAGAGAGCACACCAGTCAAATTGAATTGATTCCAT
 AGCTATTAAAACTAGGCCTTTACAGACACTGCTACTCTGCCCT
 TTGAATAAAATTAGACCAATGAATAAAACAAACAAATAAATAAATAA
 ATAGGGAAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTT
 CTTAGAACCAATGTGGCGTGGTTCTGTCAGGCGGGCTTAAGTGA
 AGGAGAGGTGAGAGAGGGCTGGCTCAACAAAGGGCTGGGATTGCC
 GAAAGGAGAGAGCTGACTGTCCTGGCTGATGGACAGGAGATCCTCTAGC
 ACTACCCTAAGGCAGGCAGTTGGGCTTGGGTAGACAACAGGAAAGTCC
 AGGCTATAGCCGTACTCAAAACCTTCTGTTCCCTCTGCCAGCC
 GGGATTGAGTCCACATTGACAGCACAGGACTCTGGTACAGCTCTTTA
 GGAAGACACAAATTGCACTGGTGAAGTCAGTTATCTCTGGCGCCTTGG
 TCCCTCCAGGAAGACGGGCTGTTCTGAGGAGTGTGATGTAC
 CAGTGGGAACCTGGCAGACTCAAATTCCAGCTGTTATTGATTCTAT
 CTTGTTGAAGACAAATGCTTTCCATCTCTCTGGTAATTGG
 GATCTACACTCTGCACTGGAAAGAGAAAGAAGAATTGTTGAGGGCAAGGG
 ACAAAATGCTATGGGAAAGATGTTCTTGGGTGGCCAGAAAGGAAACT
 GACGAGCAGGTACATGATCAGGAGCCACACTCTGAGTTGTA
 CCCCAACTTCTGTGATTATTAAAGAGCCCTCTCTTTCTAAAC
 TTAGTGCCTAAATGCTGAGGAGCATAATGAGGTGAGAATT
 GGGGGGGTGAAGGAAAGCTGGAGGTGATAGTGGTGGTGAATTGG
 GCTTTTATTGTATTCTTCTGAGTACCTAGTTCCAGGG
 ATGAAGCTTGCTGAGGAAAGCTGGAGGTGATAGTGGTGGTGAATTGG
 AGTGGAGTGGACGTGATAATGGGACCCCTTAAGTCATCTATTCCAAAGG
 TGTCTATCAAATGAGAGCAGCCCTAACAAATATAATTCTGTTGGGTTGT
 AACTATGGTAGGGACATAATAACATCGGCAAATGATTAAATTCTGCAG

CAGGATTGAAGGTTGCAGCAGTTAAAATATGTTAAATTATTTACAT
 TAATGCAGAAATTGTCAAATAGACCTGTTCCAGCTTTCTAGGGATGGG
 GGCGGGGAGAAGGTGGTCTGGGAATAAGTGGTAGCAGGAGGCTGAGA
 AGGGCTTCATTCCATAGCATTCACTTACCTCAGCTGTAGAGTGGGCTTA
 TCATCTTCAACACGCGAGCACAGGTACAGATCTTCTTGAGGCCAA
 GCCACAGGTATTTGTCAATTCTCTCTGTACAAAGGACATGG
 AGAACACCAGAAGAAAGAAGGGGTCTTGTGGTAGGGACACAGCAGT
 GCAGGGTCACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTG
 GTAGCCTCTGTGGAACCCACAGTGAGGTTCTGGCTAAGACACAGGA
 TAACTGACTTCTCACAGACAATAGCAGGGTCATTTGTTGATTAGGGT
 TTCCCCTCAAAGGCTGAGGGTTCTCAGAGCCTCATAGCAGTAGGAACG
 GAGAATGAAAGAGGGTCTACATTAAATGCTGAAGGAAGGAAGGAAGGA
 AGCCATTGTGTCACTGGCTGGCAATGTGCCCATCCACAGGAGCGAACAA
 CTTGATCAATGTGGAAAGGAAAGGAAAGAGGTGAGGCTGTACTTCTGCCAG
 AAATCAGGCACCAAGAACAGTGTTCAGGAACAGAGTAGCCCAGGGAAAGA
 AACTGGGAGAGGAGAGGCTGAGCTGGAAAGTGGCTCCAAGAGAGACAC
 TCATTGATCTTCTCAGTCACAGCAGTGCAATTGGAAAGGCCCTGGGA
 TCACTCTTACTACCCGATCAGAAAGAACAGGATTTCTGGCTGGCTG
 AGAGCAAATAGCTCCCCCTTGAGTGAGGCTGTCTCAAAGTCAGCAGC
 CTTAGTTGCCACACTCCTGTGCAGAGGCTTGGCTACTGTGGCACGATG
 CCAGGCAGATCACCACAGCTAATGATGGGTTCACCGCACTTGAAACTTT
 GCCCCTTACAGGGAGAGATAAAGTTCTGCTGGGCGGTAAATTTCCC
 TACAAGGAACCAACCTGGCATGGGACGGATGGGGCAAGGGGG
 AAGACTGGGAGGGGGATGGACACATTATCGCTCCAGCACTTTGTTCA
 GCCTCAACAAAGGAAGAGAACCCACAGGCAGTTAGGCCATGCCATC
 AAATGACCCATATTGTGGAAAGAATTGACATTGCACTATGCCAAGAGAC
 TTGGGTGGACATGGCTCTGGAGTGCTTGAGCCGTCTAATTCTCAGGGT
 CACACTCCTGTTAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATT
 CTAGGACCAAAAGTTGTATATTCTTTAAATATTTTTTCACTTGTGT
 TGATCATTGCTTAAATTAAACTTCTACTTGTGTTAAACATGGAGAAT
 TAGCAAGCTGCCAGGAAGCCAGGCAGGGAAACCAGGATGTTCCATTAC
 CTTGTTGCTCCATATCCTGCTGGAGGCTGAGGCTTCAAGTCAGTCA
 GGACAGACATCACCACAGCTTTTGCTGTGAGTCCCCGAGCGTGCAGTT
 CAGTGTACAGGTGCATCGTCACATAAGCCTCGTTATCCCATGTGT
 CGAAGAAGATAGGTTCTGAAATGTGGAGCACATGTTGTTAGGTAAAAA
 TCAGAAGGGCAGGCCTCGTGGAGGCAAGGTGGCAAATTGATTCTTGG
 GGACACCTGACATATACGGTCAAAGTGTGACAAACACCAGTAGGGAT
 GAAGCTGGAGTGGGCTAAGAACACTGGACCTGACACTATTAGACA
 TGGGTTCCAGCTTCAAGGCTATTACTGCTACTGTGGCGAGCAACAGAG
 CTACTTAGGAAATGGTGTGGTCATAACACTAGCCCACAGGGAGGTTA
 CGAACCTCTGGTACAATGTAAGTGAAGAACAGGCCCTGAGAAAGAGTGAGGG
 AGTTGCAAATGTCAGTAGCCATCAAGATCTTCTTTAAAGAATAGTTCCAC
 TAAAGAGATGATTGCTTGGTTCCAGCCTCTTGTGTTGTCTCCCCGC
 TGGGCTTCTACCTTAAAGGGCTTGGCTCTGGGGAAATTGAGTTGGCT
 GGGGCTTGTGACTTCCAAGAGGACACAAGTGGAGATCTACTGCCTGCTC
 TTGGCTAACTACCTTCTCAAAGATGAAAGGAAAGAAGGTGCTCAGGTCA
 TTCTCCTGGAAAGGTCTGTGGCAGGGAAACCAGCATCTCCTCAGCTTGT
 CATGCCACAAACTGACGCCCTGCCTGAAGCCCTGCTGTAGTGGT
 GGTGGAGATTGTAGCTGGATGCCCATCCAGAGGGCAGAGGTCCAGG
 TCCTGGAGGAGCACTGCCAGAGGAGCGAGGGAGGGAGCCTGGTGAGGTG
 GTCCTGCCAGGAACCATGCTTGTGACATCAGAGAGTAGAAAGCTCAGAGAG
 GAGGAAAGGGCTTGAAGAATCCCGAGCTTCTAAAGATCATCCCTCTG
 GGCCAGGCGTGGCTCATGCCCTGTAATCCCAGCAGCTTGGGAAGCCGA
 GGTGGATGAATCATTAGGTCAAGGACTTCAAAACAGCCTGGCCAACATG
 GCGAAACCCCTCTACTAAAAATACAAAAATTAGCTGGGTGGTGGGG
 GTGCACCTGTAATCCTAGCTATTCAAGGAGACTGAGGAAGGAGAATCGCTT
 GAACTCAGGAGGTTGGAGGATGCAAGTAAGCCAAGATTGTACCACTGCACTC
 CAGCCTGGCAACAGAGTGAGACTCTGTCTCATAAAACAAAACAA
 AACAAAACAAAATAAAATAAAATAAAAGATTATCCCTCTGTGAA
 GCTCAAGGAGGTTAAGGGTGTACTCAAGGGCACACAGCAGGTAGAGGCA

GACTCAAGACTAGAATG'GGGCTTCTGACACCTTACAGGGCTATTCTTT
 AGAATAAAATCCATTCTACTTTGTCATCTTTTGATACATGCCACC
 TACACCATACTGTATACCTCTCATATCTTTGATCCATAATGCTG
 TCACACTATGATTCGTTCTCATGCAGATGACCATAACATTTCCATT
 ACCTATGTCACTCAGCAAGTATTCAATTCTACACTGTTCTTT
 TCCTTTCTATAACACTGTCATAGGCATTGCAAATCCTGTGAGAGT
 ACTTTTGTAATGTTACACTTCCTTATTAGAGAAGCTCCGTAT
 TAAGGCTTCACTGAGGTTGCCATTAGGCATGATAATGGTCAAAGGCTG
 AAAGACAGTAAAGAGACCTGTAAGTGCACAAAAGAAAGTTGAGCAGGAG
 AGAATTCTGCTGGAGCAGAGCAAGCTACTGGAAGAGGAATGGGG
 CAAAGGCCAGGAGACAAGCCAATGGCTCCTCCACAGCTGCAGCCAAC
 AAGTATGCCAGTCTAAACTCTAAAGAAATATGTTTAACAAGATT
 GAGGACTGGATTATGAGGCTAGGGAGGCTATCACAAACTGGAATAAAAT
 AAAGCCAGAGAAAAGTGGCTGCCTCCAACCTGCACAACGTGACCTAGCTA
 GGCTGATGGCTGGCCACCTAGGAAGGCTACTGAGCATCATATAAACAG
 AAGGGACAGCAGGAATATAACATGGCTTTGTAAGGATGAGTCTGAAAAA
 ATGACCATTGCTGCCAAATGCCCTTAGCTACAACGTGAAATATTCAG
 AACTGGAGGTTGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCC
 TTATTTTCACTGAGGCTCAAAGCGGGTAAATGACTTGTCAAGGTCA
 AACAGCAAGTGAATGGTTTCTTCAGTCTCAATTCACTTTGTTA
 TATCATCTATGTTGTTATAAGCTCAGGCTAGGAGTAAACAAACT
 ATTCTACTCAAAGGGTAGACATATGTTAGTCTCAAGATCATCTCTG
 GTTTCAGAGTTAACATCAAGTGTGATGGCATAGGCTGAATCCATCTCTAA
 AAGGATAATCAAATTATGTTGAAGACTTGGTTGTCTCTACTATGAAA
 TGGGAAACATTATCACTACTCTCCCTGTCAACACCAAGTGTGGCCACC
 ACCACCAACGTTAGTGAGTGACTGTGGTGAATGATGACCAAGTGTGGCCAG
 GTCAGCAAGTGGTGCAGGCTGTCTCACTGGAAGAGGTTAAAGTCTTTC
 TAAAACAAATACCATGGCATCAAAGTGGCCAGAACACTCCCTCTTGAG
 CTTCCTGTGTTAGAGCCCTTGGGTTGGAGTTAAACCCATAGTC
 TTACCTCATGTTAGGGCCATCAGCTCAAAGAACAGTCATCCTCA
 TTGCCACTGTAATAAAACAGGGACATGTCTCAATTATGTTCTCTAAACA
 GGTTTATTTCTCCCTGTGACAAGACTTGAATGTTCTCATAAGAAACT
 GCAAACAGCCTCTCAAAGCTGCTGAAACACCTGGCAAGTTCTACA
 GTGATATGCGCAGAACAGTCCAGAAGGAGATTCTAGGCCTGGCAGGTGG
 GCACCCCTGGGTGCTCCCTGTTGGATCTGAGGCTAACCTCTAGCCCAGC
 AGAGTCAGCTAAATCTGAGCTCTCCCTCTCCCTCAAGCCACACTTGC
 AAAGGGATTCTGTATTGGGCTTGGAAATCTTCTCCCCATTGCT
 CTGAGGAAGCCCTGCAACACACATCTGGATAGCCTCCAGGTCCAAG
 GCTGGAGGGACTTGTAAAGGGAAAGTAGTCTTAAATCAGATTACTTGG
 CACCTGTTGCCACTGAAAGAGGCAATTAGGGAAAAATCTGGTCTCC
 AAGCACAGATAACACTCTACTTGAAGAGGGAGACCTGCTCATGTTACT
 GGTCTAGCGTCTCCACTGACCTGTAATAAGCCATCTTCACTGGCGAG
 CTCAGGTACTCTGCCATGGCTGTTCAAGACACCTGTGAAAAGGAGGAA
 AATGAGTGAATCCCCATGACGGCTACGTTCATGTTGATTCTCTCAGC
 ATCCAGTGCATGGCAGTCATGCAAAGAAATGATCTGAGTAAATGAATG
 AATGTTGAAAGAGAAGTCTTGGGCTAGAGAAAAGCATTTGCTAAAC
 CAAACCCAACTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTT
 GACACTAACCTTCTGGGCTAGCTTGAAGGAAAGTAAAGTCATATTGA
 GAATATTCTCGAGTCATAAGCATTATATTACACCTGGCATTTGCAA
 AAGCTGAGAGAGGGAGGAGAGAGGGAAAGGGAGAGGGAGAGACAGAGAAAG
 AAAGAGAGAGAGAGAGAATATGCATACACACAAAGAGGAGAGAGACA
 GAGAGACTCCCTAGCACCTAGTGTAAAGGAAGATTAAAGTCATATTGA
 GCAATGAAGATTGGCTGAAGAGAAATCCCAGAGCAGCTGTTGCTTGT
 GCCTCGAAGAGGTTGGTATCTGCCAGTTCTCCCTCGCTGTTTATAG
 CTTCTAAAGCAGAAGTAGGAGGCTGAGAAATTCTCTGTTGAATACCTG
 ATTTCAACATCAAGTTAAAGGAAGGGAAAAGAGTATTGGTGAAGCTT
 CTTAGGGAGGGACTAATAAACTGAGATAATTCTCTGGTTCATGGAAGG
 GCAAGGAGTAGCAAACATGACACATTGCAAATGTATCACCAGTC
 ATGCAATTGTTCTGACAATCGTTGTGCAAGTTGATGTCCACATTAAA
 TACTGGATTCTCCACGTTAGAAGAATGTTAAATTAGTATATGTGGGA

FIG. 4 (49 of 61)

103/118

CAAAGTGGAAAGACACACAGATTATACAAGCACATACTTTCTTCATTCA
 CTTCTTGTACTTAAGTTAGGAATCTTCCCACTTACAGATGGATAATG
 GGTACAATGAAGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGT
 CTCTACCTTGGGTGCTGTTCTGCCTCGGGAGCTCTGTCAATTGCAG
 GAGCCTCTGAGGAGAAAAATTGACCTTCTTGGCTGGGCCAGAGAACATAC
 GGTATGCAGGGTTCAAGGCTCCTGACGGAGTTGGGCCAACCTGGAGATAA
 GCTCACACAACCCCTGCAAGACCAGGGTGTACCCTAGCCAATCTCATG
 GATGAACCAGATCAATGCAGATGAGCTCTGCCTAAATGATTTTGTT
 GAACTCTGAAAATGGAATTATGTTCTGTAAGAATATCCATCTGAGACT
 CTATCTTGGTAATACCAAGAGTTATCAGTTCTCTTAAACCGAGACAC
 CAGCAAAGTGCCTGCTCCAGGGTACTGCCAGGGAGGCCCTCATTGTA
 GAATGAATGAGAGTCCAGGTTATGAACAGTGCTGGAGTGTAGGAACACC
 CTCCTTGCCTCTTGACAGGTCTGCATCATACACTTTTTTTTT
 TGAGACAGAGTCTCACTCTGCCCCAGGCTGGAGTGCAGTGGCACGATC
 TCGGCCCCCTGCAAGTCCGCTCCGGGTTACACCCATTCTCTGCCTC
 AGCCTCCCCAGCAGCTGGACTACAGGCACCTGCCAACGGCCGGCTAA
 TTTTGTATTTTAGTAGAGACAGGGTTTACCATGTTAGCCAGGATGG
 TCTCGATCTCTGACCTTGTGATCTGCCCTCGGCCCTCCAAAGTGT
 GGGATTACAGGGTGTGAGGCCACCGTGTCCAGCCTGTAACACTTCTTATAGC
 ACTGAGTTGAAACCTTGCTCCTGGTTCCAGGAAACTGAAATCTT
 TTTGAGCCAAGTCTAGCACAGTGCTGGCATGTACATTCAAGTGTAGAG
 TTTGCTGCTTGAATGGGTAATGGGAATTGACAGCATTATTCAAAT
 TAGTATGTGCCAGGTATCGTGCTCGCTTGCAATTATCCAAGGGAGTGTGAGC
 CTCTGTGCAAGTATTGAGACACGAGGGAAATAGGTTCTACTGTGGGAAA
 AAGAGCATTTCATGGACTTGCTCTCCAAGCAGCCTCTGATTTTAAATT
 GGCTCCCAAGTATCTGATATCAGGAGTCAGTCACAAGAACTCCATCTTA
 GTAAGTTATATTCCACAGGAAATCTAAAGCTGTTAACATGTTAGTT
 TCCTGTGAATTGATAAGCCATAATCCATTCTAACACTGAGCCCTCCTG
 AAATTGGTGTCTGGTCTGCAGATAGCTAAAGCCCTGTCTGGTGGCC
 TAGGGACTCCCTGTGTTTGCCTCACAGGATCCACTTGCAAATTAAACC
 ACTGGTTCTCCGTTGAGGAACGTGCCACCTCCTCAGAGCCTGTCTTC
 TTCCCTCCTCCTCCTCTTCTTCTTCTCTCTCTCTCTCTCTCTCT
 TCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
 TCTTTCTTTCTCCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT
 TTTCTTTCTCTCTCCCTCCCTCTCTCTCTCTCTCTCTCTCTCTCT
 TTTGTCTCCCTCCCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT
 CCTAGACAGGATCTACCTTATCCCCCAGGCTGGAGTGCAGTGGTACAAT
 CATGCATTATGCAATGATCACAGCAGCCTCAAACCCCTCAGAGTCT
 TTATCGGGCAACCAGCAGGGTCTGGAGGGTGGCTCTGTGAACCTC
 CTGACAGAACACAGAGATGTCTTGGCTGTTGATGTGATTACAAGCTGA
 ACGAAGGAGGATCAAAGCCAGTGCAGGAAGGGAGATATGCAAGGGACCC
 GAGCATCAGCTGTGAGTTAGTCCATTCTGCTCTGGACTTGGGATACAG
 GTCAGAACCTTGAGCTTCTACTTCTCCATCTCCAATTGTTAGCATCCAG
 GACCTCAGAACATGCCAGCTAACAGGGAGCCCTAATGATTGTCGGTGGGA
 TATGGTGGGACACAGAGATGAAGACATGAATAGCTATTGAAATGTGAAC
 AGCAGACGAAGAAATCAAGGCTAGGAGGGTGAAGTGAATCATCCAATAG
 CACAGTGTGGTTGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCTGAT
 GCTTCGCTGAGGGAAATTGGAGCCATGGGCCATGCCCTGACGT
 AACAGTCTCCACAGTTCTGCCATGTCATCCTGGCCCTGTAACCTGGAC
 CCAAATCTGCTACCATCCCACATCTCAGGAAGTGAACACCTCTTATGTC
 AAATAGGGTGTGCAACGTATGTATCAGATCTGTCTTCCAAAGGAGACCG
 CTCAGGCCACAGCACTCCCTCGATCCCCAATGAGCAGAAAATATCTCG
 CTATAAACATAGTTGGCACTAAGGGAGGGAGTGAAGAGTGTGATGATG
 TAGATGGTGATGTAGCCCCAAGGAAGTGGAAACAAGCAGAGATGGGAGCT
 GGAAATGCCAGGATGCTCCAGCTTGGGAAATTATTGAGTCTTGTGAGTC
 ACTAAAGCCTTCTCAGCTGCAAGTTCTCTTACCCCTGTCAGGTCATT
 TTCCAAGACAGGAGACTGACATTATTCAAAGCAGCAAGTGCCTGATAC
 CATCTTGTGCTAATCATGGCTCGCAGCAGTTATCAAGGTTGATCTC
 ATCTCATTGGCTTCAATCATTTGAACAAGAACAGCAAATAATCA

FIG. 4 (50 of 61)

104 // 118

TGGGTTAGTTCTTATATTGTGTGTACATGCAGTGATGTCTGTTCTT
 GTAGTGAGCTGTTCCCTTGTTCACCCCTTGCTTAGAACAGAACTAA
 GCAATCTGCCCAACATTTCCCCAATTCCCCTCATCTCATTCTGGCACT
 GGCTTCTTAATATTGTTCTATGAGTCATTTCTGTATCATTTCCATG
 AGTCCCCTGGGATCTTAAAGTATGAAAATGTTGTGTACCCACACCT
 GTCTTGTGGATATTCTCCTTCCCTCTGCTTCTGGATTATTGG
 GAAAGGGCACTATGATTTTATCATATCGCTCCACTTCTTTATGGCAT
 CATCTCCAATGGGCTTCTTCTCCCTTGTGGATCCAGGTTCTCAGATTGGG
 GACATGCAGAGTCCAAGGAACATTCCATTCTCTCCCTGGTCTAGAACAA
 GGAGGGCTTAGATATGAGCAGGTGGCTGGCTGGCGAGCTATGAGT
 CTCCAATGGCTTTCCCTGATGTCGGAGTTGTATGTCAGTTCTGGAGA
 CCAATAAGACCTTGTCTTCTTGGATCCATCAGAAAAGCCCCTGGGT
 GGGTAAGATGGATGGCAGGGCTCTCTACTCTATGTCCTTCTCACACCT
 AGTGGGTATAAGAGAGGGGACCACAAACAGAGGGGCTCTGGTACCACTT
 ATCCAGGGCTGGAAACATTTCTGTAAGGGCCAGATAATAAATGTTTC
 AGGTACAACACTCAACCTTGATCATTTCAGAAAAGCAGTCAGATAATA
 CATAAAATGAATGGGTGTGGACTTGTCTGGCTCCCTGTCTTATA
 TCATTGTATTATCATTTTCTTACATACAAATTAGAACATACATT
 AAAAAAAAAGCCGTCCTTATTGAGCACCTACTAAGTGCAGGTACCT
 TTTTCCCTCATTATCTTATTAACTCTTCATAATAACCTTAAAGTAGA
 TAATATTGAACCATTGACTATGCAGAAACTGAGGTTGAGACAATAAT
 TATTAAGACCGACAAACAGTAAATGCTGGAACACTAGACTCAAATATGG
 GTTAACTGAACCAAAACCAGATCTTATTCTCACTTTAATTGTTACAT
 ATGTTATTGCCTCATCTCTGTCCACATGGTGCACACTGGCAGACTCCT
 TTCTCATTCTCAGTGATTGAGTGACATTCTAAACTACATTGGCTGGCAG
 ATTACACCTCTGTCCCTAAATGTTCCACATTGTCTTTAGGATTGAGA
 TCCTCTCTGTTCCCTGTCTTCCCTTCTCTGGCGGTGACGTG
 CTGTGTGAATTGTTCTTCTCCTCAGGGTAGTACTGGACTTCCA
 AATCAGGGTTTTAATGATCTCTCNCTTCTGAATTCTCCTTAT
 TCCCATTCACTTCTCATCTATAAGTGGCANCTTGTGCTGGAAGATAT
 CCCTTGTGCAGGGATTNCTCTTAANAAATTGTCNNNACC

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GTGATCGTCAACCTCCCACCCGTAGGGCCTCAAGCATTGAGGACAATCA
 CTGGCTGCCATTAAACCCAGAAATGTTGGCGAGACAGGAGGCCGTGGCCC
 AAAGTTCTGGAATGGGTATTATTATGTCAGCACAAAGCCTTGACAA
 ATGAAGGTTTAAATGCACTGCTAGTCAGGTGGAGGGCTTATAGG
 ATTCCCAGGAATCTGGATCATTCTTGTGAGAGCTTCCCTGTCTGT
 AAAACTCACATCGTACGGCCAAATAACAACAAAAATGGATGTAATT
 TTGAAATAACTGTGGATGGGGAAACAAGGCCACCCCCCAGATCTGCCA
 GAAGCTTCAGGTGAGGGTCCAAATGCCAAAAGTCTGGTATCAGAGAGG
 ATGGCCAGTGACNTGGGACACATGCCCTTGCTGTGTCACTCAAGGAGC
 AGCAGCTCGGCCCGCACAGTGACAGGACCTGGCTCCACGCTGG
 CAGGAGCTGGTGTGATGAAGGGATGCCTGGCAGCACGTGCTGT
 CTCCTCGTGTAGCTTACCTGGCTTGCTGCGAAGAGGCCACTGCATT
 CTTTATTTTATATTTTTAATTAAATTTTTATTTTATTTA
 TTTTATTTATTATTTATTAAATTTTTAAATTAAATTATG
 CTTTAAGTTTAGGGTACATGTGCACATTGTGCAAGTTAGTTACATACGC
 ATACATGCGCCATGCTGGTGCCTGCACCCACTAACTCGTCATCTAGCAT
 TAGGTATATCTCCCAGGTTAATCCCCTCCCCCTCCCCCACCCACAAC
 AGTCCCCAGAAATGTGATGTTCCCTCTGTGTCATGTGATCTCATTGA
 ATTCTTAAAGGTGGAATCTCTCAGTGGGGCTAATCTGTTCAGAAATA
 TCAAAAGAGTATCCTGGGAATGACTGGAATTCCAGAGTCATCTGGTAAT
 CCTCATAAAACAACCTCTGGATGTCCTCAGCACATCTCCACCTTGAAC
 GCAGGAGGCTGGTCAAAATGGAGGAGCATCGCTCTACTGCACTTTTT
 TTTTTGGCCTAAAGTGCAGGAAAGGGATACTGTTCATGTAATAAATCAA
 CTGCAAATCGCTAGTTATGCTGAGCCCTGCCCCGTGCTGTGGACACAAAG
 GAACCAAAGGTTTCTCCCCGCCAACACACACATAACACACACACAC
 ATCATAAAAACATACATACCCCCAACACACATAACACACACACAC
 CAAAATATACACACACACACACACATGCCACAAACCTGTGTCC
 AAAATAATCCTACTGGTGGTTGTGGTCTCCCTAATTCAAAATGA

FIG. 4 (51 of 61)

165/118

AGCCGTGGACCTTCGCA GTGAGTGTACAGCTCTAAAGATGGCATGGAT
 CCAAAGAGTGAGCAGTAGCACAGTTACTGTGAAGAGCAAAAGGACAAAG
 CTTCCACAACCAGAAGGGGACCCAGCAGGGTTGCTGGTGGGTGGCC
 AGCTTTACTTCTTTGGCCCTCCATGTTCTGTTCCATCCTATCAG
 AGTGCCCTTTCAATCCTCCCTGTGATTGGCTACTTTAGAACCTGC
 TGATTGGTGCATTTACAGAGTGCATGGTGCCTTACAATCCCCCT
 GTAAGACAGAAAAGTTCCTGATTGGTGTGTTACAATCCTTGTAAAGA
 CAGAAAAGTCCCCAAGTCCCCACTGGACCCAGGAAGTCCACCTGGCCTC
 ACCTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACATA
 CATAACACAAAGTATACATGCATCTCCCCAAATATAACACATACCAAGAAA
 CATACACACAGGAACCTAGCTACCTGTAAAAGTCTGCATGGTATTGCC
 TCTGCAGTGGAGTAGTTAGAAAAGTGAATTGTTCAATAAATTGGAGT
 CCTTAAAATCGTTGAAGATAGAAAATTTTAAAAGTATATAAAAATAAA
 ATATGTATGTCCTTGGTCTAGCATTACACATGTAGGAATTATCCTAG
 TGGAGTAATCAATGATATATGCAAAGATTGGACAAGCATATTAAAGCACA
 GAATTATGTATGCATATGTGTGTATATATATATATCTATACATAT
 AATAATGTAAAAGTAAAATAACTCAGATGTTCAAAATTGAGGATTAGTT
 AGACTATGATCTGTCATATGTGACATACAAGTTAGCTGCCCTTATTCT
 CTCGAGCTCAACCTCCTATAAACAGTGTCCCTGTATATCAGTATTGGT
 ACAGATAATCGAACTTATTGAGGTTTACATGGGCAATAAAGGCAAGAG
 TTTATGAAATACCCATACTACACTAGGTAGCACCCCTATTAAAGAACAAA
 CTCTCTCTCTCATTTCCCTTCCGGAAACCACTGGTGAATCTCT
 ACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCGTACATCTCA
 TCTTCCCTGTCTGAGAGCAATGGCTGTCGCCCCCACTCACATCCTC
 ATTCAATTCCAGAAGTGAGCACACAGAAGTGCCTACAGTTACCCAAACCA
 CCTTCTAGAAGATAAGTTAGTGTGTTGACTTTAAAATTTCAC
 TTCTCTTTCTTCACAATCTCATCCCCTCAAGAGGTTATCAAGAA
 GTTCTCTAAAGATATGTGTCTCCTTATGGAATTAAACAGAAATCAGGGAT
 TTGTATTCTAGCCATCAAGGAATAACATTTCAGGTCTTAGACAAAA
 TAATGGAATACCTTGCA GTAAATTAGATACACTATTGTAGAAAAGTATTGA
 TGAAATGGAACGATGTTGAGATATCATATTGAGTAGAAAAGGCAAGATA
 CATTAAGTAGGAAATGTATCTTACAAAATAATTGTCAAGCACACTCCTA
 TATTGTATGTTATATAATGCGTATGTGAAGAAAAGGCTAGAGGATGAGA
 CCACAGTCTCGGTGAAGTTAAGAGATGAGGCTGCAGCATGCTCAGAAA
 GGCCTGGTTATAGTCTTCCAGTAATTAGGATGTGATCTGGTAAAT
 TGTCCATCCTCTAAACTGCACCCACCTTGTCTGTAACAGGAAGGA
 TGGTATTACCCCCAGGGTCAAAAGGATTGGTGGAGAAAATAAAT
 AAATGGGCTGAGCCCAGACCTGGCACAGTGAGAGCACAGTGGTGA
 ACTATGTCATCTGGTCTGTTCTGTGTTATTGACATGCTGCTGGTGGTCC
 AGAAGCTATTACCTTAATTGGTTATGTGGATTCCCTCATACTGAGCAG
 CTGTGTGTGGTGTAAAACATGCCATACACAGTAACGTGACAAGGGCA
 AATGTGATGAAAATGCAAGGAAGTGCAGATAATAGCTAATGGGCTGT
 AGAAGGAAGCTAGTCCTGGAGGGCTGATCAAGGAAGGTCTTGTGAT
 GTCACCTTGAAGAAGAGGGACATAGAAGAGGTATAGTGCATCCGGAG
 TGTACCTGGAAGGGACATGAAAAGAGGACATTTCCTGGACATGGG
 GACTCCACTGCATGAACTCTGGAATTGGGCAAAGAACCATCATGAGAA
 CAAGGGCTTCTGAAACCTCCAGGCTCATGGCTGATCTAAACCTGTG
 TCCCTCTTCTTCACTCTCCTGTGTTCTATACCTGTATTATTGGAC
 TGGACTGGAAAGCCACCTGATCTACACAGTACCTGAAATGTGTTGAAT
 AGGTGTGGCACAGTCCTTAGCAGAGTGGCACTACCCCCACAGGAATTG
 TTATACCTTGGCATGAAAATAGCAGGAATGAGTGTACTGATAACT
 GAGGATGCTATTATTATTGGCAAAGGAATACTTGTGTTGATTG
 AACCAACTCACAAACTGTTGATTACAATGAGTACCAAGACCTAGCTCCTC
 AAGTAAAGGATCCTGAGAACTGAAGGAAACAGAGCTCCAGGAGTCCAAG
 ACAGAGCCACAGACCACGAGGATCCCTGGCCAGGTAGGTGGTCTCCTG
 CACTGGCTTCAAGGCCAACAGGATGGATGGGAAGTAGAGTAGCATCTG
 GCCATCTAGACCCCTGCTTTTATCCCCACTGGAAGCACATCTGAATT
 TAAATATGATCTCTGAGACCTGCCAGAACACCTGTCTCAGCCCCAGT
 AGCAGCCTGCTCTCCAGGAGGGCTTCACTAACAAAGTAGGGCATTG
 TGGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCCTGGAAATG

CTAGTCCCTCTGAAGGCTCAGAAGACTGACTTAGAGTCAGAAAAT
 ATTGGTCTGGAAACAGATTTGAGTCAAAGAGATGGACTTCAGATGG
 CCAGATGCACTGCTCTTAGGAAATTCTGTGAAAGCTCCCTGCATTTAT
 CTTAATAACAGGCAGCAGATTCTAGAGTACCCCCGAGGGATGGCCCCAGG
 TCCTCCAGCTGTGAGCATCCTCTGTCTTCAGCAGCACACAGTATCT
 TTATATGTCTTGATACTACGTTCTGCCAGACATCTCTGCTCTGAT
 GTCTGGCTGCCAAATTCTCTGTCAAGCGCTCCAATTGGTGTCTT
 TGATTTACCCAAACATGACAAGGCAGTTGTCTCATGATTAGGGAT
 ACTGCCAAACCAACAAACAGGTTAAATCAAATAGCAGATATCCCTGTTCC
 TAAAGACCCATCAGCTCTACCCACCTGCTCTGTCACCCTTATTGT
 TGAGTCCTGAAGCCCTCTGTCTATTATTGGTGTGATGAAACAATT
 AGTCCCCTTGCTCTACCTCTAAACCTTCTCAAAGGATTGGATTGTAC
 ACAAAACTGCCTATCTGCAATCTAGAAGTGATATGATTCTGAACAAAT
 CACTTAACCTTGATTTTATTGGTAAGATGGAAATACCAATTGGCT
 CCACCTCTGTCTATGTTGGCTGGCTGATGTTGAAAGCTCTCGGTCAA
 CTGAGATAGGGTGTGAGAATTATATATAAAATATCTECTCCAACC
 CCTCCCAATGAAGCAAGTCAGTGAGTCATCTACCCCTAACAGATATTAGG
 GATTGAGCCTCTGGGACATTGGTGGCTTAGGTTCTATGAAAAGAGGT
 TGCAGAGCAACTGCTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACT
 CAGCAAACCTCTATAGAAGGTGTAGATGGTAAGTATTAGGTTGCT
 TGCCAGATGATCTCTCAACTAGTTAACCATGCTATTGCTTAGGCTCGAAGCA
 GCCAGAGACAATATGTAACAAAGAGCATGGCTGTGTTCAATAAAACTTT
 ATTTAAAAAAACAGTCAGGGACCGGATTGGCCAAAGGCCATAGTGTGCC
 AGCCCCAAGACTAGAGCAATGCACTTTAACCTTTATTGTTATTGTT
 AAAATGCCAAGATCCACAAAAATGCTATTGCAACCCCGTGTGACTG
 TGACTCAAGGTTGGGAAATTCTGCTTGTGAGGCGTGTGATAGACAGGAGAG
 CATGGTCTGGCCCCCTTGGTGCCTTCTGGTGCAGCGAGCATTCAAAC
 ACAGAGCAAGGCCAGTGGTCTGTCAGCACTAGAGACATGCAGCAAGGTG
 TCCCTGGGTGAGAAGATGCCATAACTGGTCCCCCTTCTATCTCTTAGGT
 CTTGGACTTCATTCCATTCTGTGAGTAATAAACTCAACGTTGAAAAT
 GTCCCTTGTGGGGAGAACTCAGGAGTGAAATGGCTCTGAGGACTGGG
 AAAAGATGAACCCAGTGCTTAGAAGGTAAGGTTCTGTAGAAATC
 TACCTCAGGGCAAAGTGTAACTCTAGAGCAGAACCTTGCTAGGTGCTG
 TGACAGACCCAGTTGTTCTGTCAGTGACAGTAAGTGAGCTTCA
 AATTCCCTGACAAATAACTAGACAAGAGAAATTCTGGAAGAGAAAAGG
 AAGCTTGCTCAGTGTCCAGGCACATCAGGTAGTAGATAAAAGGATCGT
 CCTCACCTACAGATTGGGCTTGTACATCCTGTTGCCACTGGATGGT
 TGCAATGCTCAAATGCACCTCTCCCTCCAACATTCCAAGTGGAA
 GAGAAGCCTCCGATGAGAAGGAACCTCTAAGGCTGGCTGAACAAATGA
 CCCAGGCACAGGGCATCTGAGTATTCCATGAGGAACACATTGGGTGTTG
 CCCATGGGACAATAGGAGGAGGCTTGACCCAAATGATTGTACTG
 AGGTGTGACGGAGAGGCCTGTGACATGCCAGAGGCCAAACCGTGTAC
 AGTCATCTCTATTCTATGTTCTGAAGAGGGAAAGCTATGATTAAATGTC
 ATTACTATCATGCTCTAGTATTCTCAGCACATACACAGAAGAGGGA
 ATTAAATGGTCTTGATAACCCCTAAATCCTGGAAATCCGAATTGCA
 TGCTAACCTCACTGCGTCTGACTGCAAGACCCGGCTGTAAGCCCCCTGGAA
 CCAGGCCAAGCCTCCCCGCCATGAATTGGTTCACACAAGTAAGGCTC
 GGGGTGAGGTGATGGGGTGGCTGAGGTGCGAGGGTGGGATGGGGATG
 GAGCCATTGGGTCTTACAGGGTGAGAGAATTGAGAATGGGACACC
 TAAGGGTGCTGGATGGGGCTGAAGTCTTCTTGTGAGAAGCAAATCCA
 TTAGGAGATAACTCTGGAAAGATGAGGCCGGGAGGGCAGGTGATGCT
 CACCTGCTAAAGAGGCAAAGGGCAAGGAAGAGTTGTGCTGGAACCTTC
 CAGGTGCCTCTGACCATAGCCAAGAGACTGGAGACACAGACCTCTC
 CCAGCACTGAGGACAAACAGCCATGGGCCAGTGGGGTGCAGGGACACC
 CACACCACTAAGGGCTAGGGCGGCCCTCAGAGCCTGAACCTCTCT
 CATGCTGCCATTGAAACACCACAAACCCCTAATAGGAAACTGTTAACATT
 GCCACTGTTAGGTGTGAAACCGAGACAGACAGTGGAGATTCCCTGCC
 TAGGTGACACAGGTAAAGTGAACAGATGTGAAATTAAAGGTACTATA
 ACGTCTGCTGCTGACTCAGGCTTAAGGCTCCATCACCTCTTCT
 AGGACAGAGTCAGGAGGCCAGCCTGAGCCCCAGCTTAGTGCAGGTTC

FIG. 4 (53 of 61)

107 / 118

ATGTGGGAATACTGAGC CCACTAGTAC ATGGCAGAGAGGACCAAAATGG
 GACCAGGTGTGAAGGGCTGGCACAGTTGGGGAGGCTGCTGCGCT
 TCTCCACCGCTGCTGCAGTTACCTTGATGTTAGTTTGTGTTAG
 TTACACCATTGCTGGCTTGGATCTGCACTGTGTCACCTCCAGGTGGAAC
 CACGCACACAAGCCTCTGTGGCCTGTACTTCTCCGTGAGG
 GCTGGGATCTCCTCAAATCTGGCGGAAGTGGTTCTCCAAGTCTGGCCT
 CAACAGTCAGCAGCATCAGCGCTAGAAGTGTAGGAATAACACATTCCA
 GGCCCCACACAGACCTCCTGCCTCAGAAACTCAGGGCCTGAGGCTTA
 GGGGCTGTTAACAAAGCCTCCAGGTTATCGTGACGCCACCTGAAAGTC
 TGAGAGCTACTGCCCTACAGAAAGTTACTAGTGCCTAAAGCTGGCGTG
 GCACTGATGTTACTGCTGCTGTTGGAGTACAACCTCCCTATAGAAAACAA
 CTGCCAGCACCTTAAGACCAACTCACACCTCAGAGTGGCCTGAGAAAGA
 TTTGGGGTCAAGGATCATGAGCGAGAACACCAACTTAAGAGGATAGTGAAC
 TAGTCTGCATGTGAGACGCTGAGATCCTATGTCAGGCTGTGATAGGAGGG
 AAACAGAAACCAAAGGAAAGAACAGCTTAAGAAGCGCTTAAGAGGATACA
 AAGTAAAATGATGGTCTAGAAAAGTAGCTTCTTAAAGAGCATTTC
 AGTCTCACCTGGACTAACTGAATGAGAATCTCAGGAGTGTGAGGCCAG
 GTATCCATGGCTTAAATGCCACCCACCAGGTGATTCCCAGTGTGACC
 AGGGGTGAGAGTCACAGCCTTAGGCCATGCCACTCAAAGGGTGTCTCAG
 ACCAGCAGCACCCACAGCTCTGGGAGTGCATCAGAAAGACAGAGGCTTGG
 CACCAACCCACACTGAACCATGTTGAGGTGATTCTTGACATT
 AAAGTGTGGAAAATGGAAAAGCTTAGAGTTAGCTAGCTAGCTCGGTGACTCTC
 AGTCAACCTGCACCTGCTCCATGAACACTCAGACTGCCCTGGATGGCCAG
 AAAAGCTCTGAGGAGATTCTGATGTAAGGCAGGGCTGATAACCATGGAT
 CTCATCTGACCCCATATCAGTGGGAGTTACTTAGGATCTTGCCCTGGG
 CAGTCATCTCTCCATAGACACTGAGAGTGTCCACGATGCTTGGGCACT
 ACAGGGTGGGAGGTGGAGGATCACGGGTGAGTCAGATAGGAAGCCTGCTC
 CTGGGGAGCTTACAGTGTATAGGGCAGCAAGCCAAGGATGCCAATACCT
 GTGTGAGGTACCACTGAGCAGTGCAGAGCCCTGAGCACCAGAGAGGAA
 GCTACCCCTGTGAGGGGGCTGAGGAGGGCTGAGGGAGATGACAGGAA
 AGCCGGTGTACAGGAGGAGTCTCCCCACTCTTGGCATGAGGAGACC
 AGGAGGACATTCTACAGTGAAGAACCCAGGCAGAGGCCATGTGCTTATGG
 CATGGGAAAAGAATGACACCTTAGACTTATCTCTACATTAGAATTG
 ACCACAGATACCCATATTATAGCTTCACATAGTGTGGTGGTTACTGTGTT
 TTCATATTGTCACATTGCACTTCCAGCCACCCACCCATTCTGACAG
 TCACTGGCCACGCTGGGGCCCTGTTCTTCAAAACAAGTGCCTGAG
 CTCTTGCAAGGGTGAAGGTGACCTGTCATCAGAGGCCAGGGAGGAAAC
 GTTCCCTTTAAGACCCACTCTAGGCAGGCCCTGGCCAAATGAGTTGCT
 AGGAGCCCACGCCCTAAGAACCCCTTGAGCACTGTTGCTGGCTGCTG
 TGCTAGAAGTGTCTCCAGGGCCAGGTGCAAGATTGTGGCTTTCAA
 AGGAGCCACTAAAGCTCAGCTAGCCCTGACGGTGCTGGCTCCCTGG
 GGCTCCTGCCTCCAACCCCTCCAACTCTTCCATCACCGCTCCCTAGCC
 TGGCCAGTGCAGGGATCTGTTCCACTCTAGGCAGTGTGAGGGAAATGATG
 CCTCCAGTCAGAGGGTGCAGGGAGAGTAAAGAAAACAATGATTATA
 AAAAGCTCTTTTATACGCCAGACATTCTTGTCTCAGGCTAAGTGTCA
 CTTATTGAGTAAGCATTTAGTCTCATAACTCCTCTCAAGTAGGTG
 CTGCTATTACTTCATTACAGATGAGGACATTGAGGTTGGAGAGACT
 TAGTAACTTGTCTCTGTCTACAGCAGAGCTGGGATTGAATCTATCTG
 TCCAAATCTGAAACCCATTGCTGCACAGAAAGCTTAATTGCTTGTCCC
 AGCAAGATAGAAAGCCTGGAGTGAAGAAATATTCACTGTTGCTGTGATGT
 CTGAGCCACAGGCAGGGTGGAGAGCTAGGGCTGGGCCCTGGACGTGG
 GGAAGAAAGGGCTGAGTCTCCATTTCATGTGAAGTGTGATATCTGG
 TGATATTGATCTAGGTCAAAGGTGAAGAACCTAAACCGAAGAAATTCA
 GCATTGATGACCAGGATCACAAAGTACTGGCCTGGACTCTGGAAATCTC
 ATAGCAGTTCAGATAAAACTACATACGCCAGGTGACTCTCAGTTTG
 GCTGTGTTCTGCCTCCACCTAGCAGGGGTAAGGCTCTGCTAGGTGG
 GCTCAACTCCATGCTATACCATGCCCATCTCCAGCAGGTGGTGGAGCG
 AGGAGGAGAGGCCAGGGACTAGGGCATCAGATGAAGGGTCTCTAGCAA
 TGACCAGATCTGAAAGTAGTCTTCTGAAAGGGCTGGAGAAAAGAAGGA
 GGCAGACACTAGACTGGAAGAAGAGGAGGCTAAACCGGTGATGGAG

FIG. 4 (54 of 61)

GGAGAAAGTGGACCACAGAGTCAGGGAGAGGGACTGTGCATCAGGCCTGA
 AACCCCGAGACAGGAGAGACCTTCCCTGCTCTCAGAACCCACACATG
 TTCTGACTGTCTTTCCAGAGATCTCTTGCAATTAGCCTCATCCTTGA
 GCTCAGCCTCTCGGGAGAAAAGGAAGTCCGATTCTCCTGGGGGTCTCTAAA
 GGGGAGTTTGTCTACTGTGACAAGGATAAAGGACAAAGTCATCCATC
 CCTTCAGCTGAAGGTGAGAGTTCTAGCTCAGTTCCCTGGCCTTGGCTA
 CCCCCAAAGTAAAAGGCCAAGATCCTCAATGCTCTCGCTTCTGCAAAT
 TCTTATCTTGGCCAATATAACAGGGACATCCACCTTCTGGAAGCACCAG
 GCAGAAGAGCCCCATAACTTCTTCTGGTCTTGCCTCTAGGGAA
 GGAGGAGAGACTCCTCACAGCGGGAGACAGCAAGGAGCTGAGCACCTGT
 TCTCCTCTCTGGGCTCACTGGTCTGGCCCTGGCGGGTGGCGGTCCCC
 TCCTGCTGTGGCCCTCCATGTGGCAAGCAACACAATTGGGCCAGGACCC
 GCGTGTGTGTAGGGTAGGGAGGTGTGAGGGAGCAGTCGGAGGGCAGT
 GTGTCTGCCCTGCAAATTAGTCTGGATGGAGCATCCTTCACTTGAGG
 GGAGAAATCTTAGGAAGCTGAATTAGATAACAGATCTAACCCATATTCTCT
 AATTAAAACATAGAGCTGAGATTGGTATCCATCTGACTCTTACG
 TCTCTCTCTCTCTCTCAGTTTATTAAATCTGGGGACA
 AGAAGGCCCTGGAAAAGAGGGCATGATTGCTTATCATCCCTAAATACCAG
 TACCAAGGCTGACACGTCTTCCCAGGACATCTGCCTTCTCT
 TTCCTCTCTCTGTGTAAGGCCCTGGAGGATGAGCACATGTGCTGTGTT
 TTCCCTCTCTCAAAGCCGTGCTATCTAATTAAATCCCTTACCTACA
 GAAGGAGAAACTGATGAAGCTGGCTGCCAAAAGGAATCAGCACGCCGC
 CCTTCATCTTATAGGGCTCAGGGCTCTGGAACATGCTGGAGTCG
 GCGGCTCACCCGGATGGTCTGACCTCTGCAATTGTAATGCC
 TGTTGGGGTGAAGATAAATTGAGAACAGGAAACACATTGAATTTCAT
 TTCAACCAGTTGCAAAGCTGAAATGAGCCCCAGTGAGGTCAAGCGATTAG
 GAAACTGCCCATGAAACGCCCTCTCGCTAATTGAACTAATTGTATAAA
 AAACACCAAACCTGCTCACTAAACTTCTGCTATTGGGTTCTTCA
 TTCATGCTTAAGGATTGTGTTTGTGATAGCAAGAACAGCTGTT
 ATTACAAAGTTCTGGGTTGAAAGAGAACCGGCTCTGCTTGTACTGCT
 ACCCTGAACCATCAGACATGCATGTGTGTCATATGCTATGATGTGCC
 AGTCTGAGTCAACTTGAGCAGGGAGCAGCTGGGTGATGCTGT
 GCTCTAGAATTAGTCTTCTACTGGGTTGGTAGATTCTGAGGGCATT
 GATCCTGGGCAGAAGTGGCTGAGTCTGTCTAGGGTACAGTGTGCAAG
 AAAGAAATGTAACAGCAAGTCACAATCCAGCCAAGTGTAGTGGAAAAGG
 GGTAGTTAGGCTCCAGATAAGGAGCAGGGTACTGACCTGTGGGAAAGG
 CACAGAGACAAGGAATCTGGGTAGATGACAGCCAGGAGACCAGGTGAGG
 GAGGAGCCAGGTACTGCTGGGAGGCTGTCAACAAGGGCATGGCTT
 CACTAAGCAGGGCTCAGATCCTCATATAATGGGGAGTGAAGGCTGGCGA
 ACAGAAATCAGGGCTGAAACAGAGTGAAGGGGTGGAGACAGGAGACTG
 AGGCTGGAAATTAGTTATTAGTTAGCTCTCAGTTACAAGCAATAA
 TAATAGCTTAGCTTATTAAAGCAACAAGTATACTACAAAAGGAGCTT
 CTAGAAGGATATTGGGTATATTCAATTCTACTGCTGTGTAACAAATT
 CCACCAACTTAGTGGTTAAACAATGCAATGTATTATCTGAGTTATGG
 AGGTCAGTCTGGAATGTGCTCACTGGGCAAATCAAAGTATCAGCAGG
 ATAGCATTGCTTGGGAGGCTCTAGGGAGAGTCATTTCTGCCTT
 CCAGCTCCAGAGGCCACCTGCATTCTGGCTAGTGGCCACTCCATC
 TTCGCTGCTGGTTTCTCACACTGCTTGTGTCAGCCCTCTGCCTT
 CCTCTTACATATAAGAACGCTGCAATTACATCAGGCTCACGTCAAT
 ATCCAGGATACTCTCCGCTCAAAGAGGCTTAACCTTAATCACAGATGC
 AAAGTCCCTTTGCTATGTGTCAGTAACTACACAGGGTCTGGGATTA
 GAATGTGGACATTTCGGGTGCCATTATTCTGCTATCATGTGAAAGTAA
 CTTCAAAATGGAAAGACATGCTGAAGAAAAGTCAGGGATTCTGGCAG
 GCCAGAAATGACAGAAGGCAGAAAACGTTGGCTTCACTCAGATGGGT
 AAGAGCCAATCATGCTTTGTCAAGTTAGCAAAAGATTGAGATCCAAGC
 AAAGCATGCAACTGCCCTAGTTGGGTCACTGTGTCAGTCCTGGTCA
 GAAGGGCAGCACACCTGATCAAAACTCCCTCCAAGACTGTATCCAACGA
 GGCCAGTGTGTTCTCAAAGCAGAGCTAGAGAGCTAATCCCAGGAGAGA
 GGCGTGTGGGTGGGAGGAAGACAAAGCTCAGCCGTAAGGGAGTAGT
 AGGGACAGCACCCCTAGGCATGGAGGCTCAAGTGAAGATGATACCCATGGGA

AAAGCTCTGATAAGGTCAGCTCCTCTGTTCTGATCCTGATGGTGATGG
TGATCAACACCAGCCCAGTGACAAAAAAAGTACATAGTATATTAGTAGAT
GTTTCCCACACAGAGAAATGGTAAATATTCAAGGCAGGAAACTCCAAA
CATCCTACCTTGATCATTACACATTCCGTGATGTAATGAGTACTTGCAT
GTATGCCATAAATATGTGAAATATTATGATCACTATATAAAAGAAAAAA
AAATGTGCCAGGTGACATCCATAAATTTGGAGAGGAAGGCATGCTTCTT
CATATAATCACAACAAACTATTTCACAACAAAGACACAGCTGTTCAAATTA
GTCTCTGAGCCCCGGCTGTCATGGCAGTGAGGACTCTGGTCCCTTAC
AGACTAGCAGAAAGGAGATGGGGCTTACTGACCACGGCCTTGAGGAGGCT
GAACATGCAGGCCAAATGGAGACACAGACAGCCTGGCTTGGTCTGCTC
CATCCCCTCCAACCTGATGAGATATAGTGAGTCACTATGACGTGGTCA
CTCATGCTTCTGTGAGGCTCCACCAAGACAGCAAGTGCATCAACACCTT
ACGGAAGCACAAGGCCCTGTTGTTGACTTCATGAAAGGCATGGTG
TGGTGATCGCATTGAGTAGGCTTGGGTGAGAGGTGAAAAACCCAACT
ATCATGCATTGCGAGCCCTCTGGTGAAACTGTGCTTCAGGCTCTAAATTT
CAGGCTCTAGACTGACTCCAGGATGAGTATTGGAAGCTGAAGTCAATCT
GTGGTCTCTTCTCTGTAGAGCAGGAGTCAGCACTTTCATAGAGTGCCA
GATTCTATATACCTGCCACATGCTCTGTTACAGAACAAAGAAGGCC
ATAGACAGCATGGCTGTGGCAAATACACAAAACAGGCAATAAGCTGT
ATTTGGCCTTAGGCTGCAGTTGCCAACCCCTGCACTAACACAGAGCTT
AAAGGTGGTGGTGTGCTGGAGCTAGCTTATATCAGCTTGCATAGCC
AATTGCTAACATCTCTCCAAACTCTGTGCTGTGCTTCAGCAGTGT
TTGAAATTGGCTACCCCTTAATGCTGCAATCTTCTCACTCTAACATGCTGT
CTACTGACTCCCCCTTGCCTGTCTTATTTCTCACTCTAACATGCTGT
ATAGTTTCTTCTTACATTATGTTGCTCTTCACTAGCAGTGT
CCCACAAGTCTTGTGCTGTGATGCTCCAGGCTGCTTGCAGTGTG
TGGCACTTGTAGGAACTCCATAAGATTTTATAAATGAAAGAAAGGAAGAA
AAAAGAGAGGGAGGGAAAAGGAAGGAAAGCCTCTTAAATGATGGC
CTTCTCCATATTCTATAGTAATATGACTTCCCTTGCAAAGGGGATGCA
TTTGAAATGTGTATAAATAACTCAGGTGGTTTGAAATTCTATTTC
CTAACTGTAATTGTAATCATTGGCTTATGTTAGTGAAAAAGTTTGG
CCCTTATGCCCTCACACCTGAGAATCCCAAAGTATTGGTTGTTAGAGCTC
CCATAGAGAACATAACTGGTGGCTTAAACAAACAGAAATGTATGTC
TCCTGGTTCAAGGAGGCCAAAGTCTGAACCTCAGGTGTGGTCATTCTGA
GAGCTCTGAGAGAGAACCTGTTCCAGGCTCCCTCAGTTGTGGTAGCT
CCAGGGTCTGGCTGGCAGCAAAACTCCAGTCCTGCCCTCATCT
TCACATGACTGCTCTCTGTGTTCTGTGTCAGATTGCTTCTATAAG
GACAGAGTCATACTGAATTAGGGCTCACTCGAATGACTTCATCTTAAGTT
GAACGTATCTGAAAGACCTTATTCCAAGTAAGGTCAACATTACAGCT
ACTGGGGTAGGGACCTAACATCTTTGGGGACATAATTCAACTC
ATAATACCAACATGATAACTGTTCATCCATGAAATTAAATGTCCTCA
AAAGGTGATCTCAGGGCATTAAATCTGTGACAGAAACTCCCATAGGAAC
ATTCCAACCAGAAGCTCTTCACTGGTCACTCCCTACCCATCC
GAGGTCTGGGAGGGTCAAGGAGCAAGAAGAAGGCTGTC
GGGTGAGAAAGAGAACCCCTATTCAACCCGCACTCTGTTCATGAATG
AGCTATCCAGCATAGGATATAAAATCGCTTAAAGGTGGTAGACTCCA
AACATTTTTGGTCCAGTTATCCTAATCAATTAAACAAACTCTAGAAC
CCATCTGAAGTGCAGGCATTGGACATTATGAAACTTACACAGAAC
AAAATTACAAGGGCTAAATAAAACAGGTCTGACATCTAATATTCTT
CCACATCCCATGCACTGTCGGCTCAACCCTCCACCTC
ATCCTGGTGGACACATGCCAGTGATGTCAGCTGGTCACAGGGGGC
TGGTGATGGTGGATATACAGCTTGGCAATTCCATGGCATAACTACTC
CAAATATGGCCAATTCAAACATGAAAGGCACAGACACAGAGTT
TGGAAAGAGATGTTAGCAATTGGCTATTGCAAGCTGATATAAGCTAGCTCC
AGCACAGCACCCAGCTACCTTAAGCTCTTGTGTTAGTGCAGGGTTG
GCAAACAGCAGCTAAAGGCCAAATACAGCTTACTGCCTGTTGTG
TTGCCAACACAGGCATGCTGTATGGCCTCTTGTGTAACAACAG
AGCATGTGGCAGGATATAGAAATCTGGCAGTCTTAAATAAGTGTGACT
CCTGCTCTACAGGAGAACACAGATTGCTTCACTCCAAACATTCT
CTGAGTCAGTCTAGAGCCTGAAATTAGACTGAAGCACAGTTCCACCAG

AGGGCTGCAATGCATGA:AGTTGGGGTTTCACCTCTACCCAAAAGCCT
 ACTCAATTTCCTACTGCAAAACATGTTATCATCATTATTTTACTTAG
 CCCACCTTCCTTGGCAATTTCATAGGAAAATGCATTCTAAATTCAA
 CTAATCAGGGACTTGGAGCCTCTGGACACCCCCCTGTTCTGCCACA
 GTCCCTTGAGAAGGTGCTTATCAGAGCGCTCCATGCAGGGCTCAGG
 ACAGGATCAGATGTCAGTTGCACCAAGGGCAGGGACAGATCCTCTG
 CTGACCATGCAAGGGACTGTTCACTGCACCGTCACTGGTCTGGTATT
 TCTGGTCCATAAGGGATTTCACATGCATCGGTGATTGTACATCAGC
 ACAAACACTGTGAGGAAGGCAGAGTGAGAATTGTGTGCCATTATAGG
 TGAGAAAAACAGATGCAGAGACATTAAGTAACCTCACACAGTCATGCCGG
 TTTTAAGTGGCAGACTTCAGGTGTTGACTCCTAGTCCAGAGTTCTT
 GCACTGCCCTGAGGTGCTAAACTCTACTGTGCTTAAGACTCACTGG
 GGAGCTTCTAAAAAGAGAGATTGCACAACTGAGATTCTGTTAACTG
 TTTGGGATGTAGCTCAGGGATCTAGCTGCCCTAAAAAAACTCCCA
 AGTAATTCTGATGCAAGCGTTCTTTTGCCACCTTGAAGAAACACT
 GCCTCCTCCCCATACATTCTAGAAAATGGTAACATGTTTCAGCCT
 GAGGCCATTCTGGGTGACCGGACGTCGGCAGGCCGCTGTACTAGCTT
 CAGTCTAGGCTTAAACACACATGATAGGAGATGTCCTACTCCAGATGATA
 TGAGTCTGAACCATGGAAAAATTCCATTGTTGACATCTGGTGGGTGT
 GCACTGTCCCCAGCAGTGAGGCACCCAGTGAAGACAGCAGCTGGGAGAGG
 CTTAGTTACATGCAGTGGACAGTGTGGCTAGACTGTCAGGCCCTCTGC
 AGTTACTCTGTGTCAGGCAATGAGGTGAAAGGCTGATCAGACCCACGT
 GCAGACCATAACCTCCAGGGAGACAGATATCAGTCAGGACAACCCAAGT
 GTAGCTGGAGAAGCAGTGCCAGGTATGACGGATGTATCCAACCAGG
 AAATCTGCATATAATAAGAGGAGAAAATGAAACAGATGTTGCTTTAT
 ATGTAGATATTATGAAGAGCATATAATTGTTGTTGTTGTTAAGAA
 GTTTATAAGTATGCCTTAAAATGTATAGTATATACTGTAGGTATTTT
 CCATTAGATATTGTTTCTACTTATCACATTGACATTGTAGCAAC
 AGTATAATATAACAACCCCTCTACAAAGCAGAAGGAAGTGAAGCTTG
 GAAGGAAGCACCAGTGAAGCTGCCCTTCAGGTGGGTGCAGTGAGCAG
 GAGTCAGTGAGGTTGAGATCCTTGAGAGGAGGCAATCATTAACCAGGAA
 ATCTGCACTGCATCCTGGCACACCTAACCTTGGACAATGGTCTTGG
 GCGCCTTCCAGCTTTAAGGCTTGCATTCTCTCACTCTCACCC
 ACGATGATTAATCTTCTCCTACAGAGTGGACAATAAGCCTTGAGTTC
 CTGCCTCCCCGGTGTGATCACGAGGCACTAGACATGCCAGGAACATGTA
 GGTGCTTGAAGACTGAACAAGTTAGTAAATTCAACCTCATTCAAC
 CACCACTAAAATGGGATAATAATAAACCTATTACATAGGGTTGACAA
 GAGGAGTAAAGAGGGATTCAATGAAAGTTGTTATTACATTGTTAGTAG
 CAGTGTGATAATATCAACTGAAAGTTCACTTACATTAGTAGCAGTA
 TTGATAACCCCTTTCTGTGCTTCTCACTGGTGGGCCAGGGCCATCAG
 CAATGCCAGGGTGTATGGATCTGCTGCATGGCACCAGCTGTGTC
 AATGGTGAGAACAGTACAAGGGGGCAGGGCAAGGCAGGAAGCACCAG
 GAGCAGCAGCTTCACTGGGTGAAGATGTCAGGAGCTAGGGACAGTCAGA
 GCGGGTGTGCCTCTTGTGGAGCCTTCTGCGTGGGTAGGAACGTGTC
 CAGCTGTGGCCATGGATTCACCTGAATATGGGTGAAATTAGGCATTCA
 TGGGTTAGCTGTGCTAGAAGGAGGAACCTAAACTGAGAACTGTCCCT
 ATTGCCACCTCTGATAGGCAGATGATCCATCCATCAGTGGCTGAGCTGAG
 GTGTGCACTGGGATGGTAAGAGGCCACACACAGGGCTGATGACTGAGTC
 TATTAGAACATAGATGTAAGATGTTGATAATGTAAGATGTTGATAGATTA
 TTTGTCATTAGAAATGGTACCATATAATTATATATACATAAACATG
 TATACATATAACACACATACATGTTGTTGATAAACACACACAGTATTGTC
 CCCTACTCATCCATAAACCTGATGCCTTAGCTGGGATTCCCAGCTTTC
 ACTCTCCTCTGTCACTGCTGCTATATCCTCCCCATCTGTAATTCT
 GGCTTATATGCCACTTCCCTAAAGCCCTCCCTCAATCCCTGCTGG
 AGTGACATTTCCTCTTGAGCTGCCCTGCTTGTGCTTGGTGGAGGTCA
 GCTGTATTGCACTACCTTGTATTGTTGTTGTCACATCATGTTAGAATT
 AATTCTGACACATTCCGTATTTCAAAGGGCTAGTGTGGGCTTTAA
 CAGTAACCTACGCCACACGCCAGTTAATTGTTGTTGGTGGAGA
 CAAGGTTTCAACATGTTGGCCGGCTGGTTGAACTCCTGACTCAGGT
 GATCTGTCTGCCTCAGCCTCTGGAGTGCAGGATTGCAAGGCATGAGCCA

CTGCACCCAGCCACCTATCAAATTTAAGTGCCATTTCATTTTATT
 TTTGTAGAAATGGACAAGCTGATCGAAAATTACATGGAATTGCAGGA
 GGTTCCAATAGCCAAAACAATCTGAAAAAGAAGAACAAAGTTGGAGGA
 TTTACACTTCCAGTTCAAGACTTAGCTCTAGCTACAAAGCTACAGTA
 ATCAGAACACTATGGCTCTGGATAAGTGTGCTGGACAGGTGAGCCCCA
 AAGTGGGACTTAACCTGTGAAGGTTCTGGCCTTGGCCAGGAAGGAATT
 AAAGGCAAGCCAATGGGACAAGAAACAGCTTATTGAAGGGCAGTATT
 ACAGCTCCAGCCCTGTTACAGCTCAGCCCTGTTACAACACTGACTACTC
 CTGCACAGAAGGGTACCTGTAGGCAGAGTAGCAACTCAGGGCAGTT
 TTGAGTCATTATATCCACTTTAACACATGCAGATTAAGGGACAATT
 ATGCAGAAATTCTACGGAATTGGTAATAACTTTGGTCATGGAGTCAT
 CATGGAAGGGGGCGGGGAACCTCCCTGGTGTGCCATGATGACGGTAAAC
 TGATATGGCGACTGGTGGGTATGTCACATGAAAAGCTCCCTCCACCCCA
 GCCCTGTTCAATTAGTCCTCGGTTGGTCCAGTGTCCAAGTCCTGCC
 CAGAGTCAGTCCCACCCCTACCTCTTAAGGAGAGATGTAATACATGG
 AATAGAATTGAGAGTCCAGAAATACTCATACATCTATGATCAATTGAT
 TTTCAGCAAAGGTGCAAGACCATTCAATGAGGGAAAGAATCATATT
 TTCAACAAATGGTGTGGATAACCACATGTGAAAGAATGCAACTGGGCC
 TTATCTCACACCATATAACAGAAATTAACTCAAATGGCTAAACACTTAC
 ATGTAAGAGCTAAACTATAATTCTAGAAGAAAACAGGGATATATCT
 TTATGACCTTGATTGCTGGCTGATTCTAAATGACACTGAAAGCACAA
 GCAACAAAAGAAAAAAATAGGTAATTGGACCTCATCAAATTAAAA
 CTTTATGCTGGGTGCACACCTGTAATCCCAGCACTTGGGAGGGTGTAGG
 CAGGAGGATCTTGAGGCCAAGAAGCTGAGGCTACAGTGAGCCGAAATT
 GTGCCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCCTGTCTCGAATA
 AATAAAATAACAAATATAATTATAGATCTCTGGATCTGCCTCGGAG
 ACTGACTCAACTAACTGGTCTGGGAGGCCAGCCATTGTTATTTT
 GAAAACCTCCAAATGATTACTGTGCAAGGTTGAGAATCACTGT
 ATCATAGGGTGGACTCTAACTGGAAACAGTTGCACCATCAGGTGTCG
 CAGCATTCTGATAATAGTTAAGCTTCTCTAGATTCTGATATTAGA
 TGAGTCATGTTACAAGTTTACCAAGAGACAAACTATCTTCTGCC
 TACTTCTCTTATACTATTCTAACTCCAGAACCTTGGAACTCCAC
 TGAGAGATGAACTAGAAAGTACTCTTGGCTACAACAGAGAGTAATG
 TTGGCTGTTGCCCCGAGATCCAGTTGGTGTGGGGACAGCACCT
 CCCTGAAATCCCCTCTCCCGTCAGATTGAGTCCCCCATTTGATCAC
 GTACAATCATCACTATGGGTTCTATTACCTTGTAGGGCATTTGGAGGT
 ACCATATACCAACTATTAGTTGAGCATGGTCCAAAGTGTGGAC
 TGAGGGCACCTCAGCACACTCACGAGGTGTGATGGGATATTAAATATT
 CTGAAGAAAACACAGTGACATCTGTGAGGCCGAGGCTGAAAACCGTGGCATT
 AAATGTCACCCAAATTGCTTAAGAAGCAGAACTGGCCAGGCACGGTG
 GCTCACATCTGTAATCCCAGCACTTGGGAGGCCGAGGCGGGCAGATCAC
 GAGGTCAAGGAGGTCGAGACCAGCCTGACCAACATAGTGAAACCCGTCTC
 TACTAAAATATAAAATAGCCATGCACTGGTGGCATGCACCTGTAACCC
 CAGCTACTCAGGAGGCTGAGGAGAGAATTGCTTGAACCTGGAAAGCGG
 AGGTTGAGTGAGCCAAAATCGTGCCTGCACTGCACCTGAGCTTGGGTGATAG
 TGAGACTACATCTAAAAAAATAGCCATGGCATGAGAGAGAGAGAGAAGCAGA
 ACCATCAGGTGTTCTTTGGCTTAAAGTACTCTGTGAGGAAATTCTGG
 GACACGAAGGATACCATGAACTGAGGAGATTGGGAAACCTCTGCTT
 AGCTGGAGGTAGCATTGCTGGGACAGTACTGCCTGGGATCAGCAAAT
 CCTTTGATGGTGCATTAGGTGTGGCAAGACAGCTTGTAGAGTGGGAC
 GGGATGTGCTGGAGACAGAGGGAACTAGATGAGGCTGCCCCGATAAGAC
 ATGCCAGCCTGGCAGAGTGTAGTCACTGTCATGTAATCCTAGTGCTT
 GGGAGGCTGAAGTGGGAGGATTGCTTGAGGCCAGGGTTGAGATCAGCC
 TGGGAAACAACAAGACTCTACAAAAAAAGAAAAAAATTAAACCA
 CATGTGGTGCATGCACCTGTAAGTCCAGCTACCTGGCAGGCTGAGGTAG
 GAGGATCACTTGAGGCCAGGAAGGATAACATTGAGGCCATGACTGTG
 CCACTGCACCTAGCCTGGGTGACAGAAAGAGACTCTGTCTCAGAAATAA
 ATTAAATAAAATAATATAGTGGCATGACATCCCTAGAAAGACA
 AGGTCTGGGAATAGGTAGAAGCCAAGGGAAATGAGGAAATGAGGAGGGGC
 CCTGGAGCTGGAACTGGGGAGCAGGATGGCCTCTGAGAAGTCTGATA

GTGGTGTCACTGATGTGTCAGTTAGTTGTAATTATTGCTGGGCC
 CTGTCATCCCTCATATCTGATAGCTCTTGCTAGTCAGGAGCTGG
 GGATCAGCGGCATCAGCATCACTGAGAACCTGTTAGAGATGCAGAATCT
 AGAGCCCCACCCGGGACCCAGAAACAGAGCCTGCATTAAACAAGCTCCC
 CAGGTGATTCTCACACACACTCGCATTGAGAAGCAGCTGGCTAGTTGAC
 AGATTCTCAGGCATGGCTGACATTGAAATATCCAGGGAGCAGGCTGGCA
 TTAGGATGTTAAAAGTCTCCAGGTGTTCTAAAGCCAGGTTGAGGAA
 TTACTGGGCTGATACAAATGTTTGTGATGATGCTTGTGTGTGTG
 TG
 TGGTCACTTGGCACCAACACAGGAAACATGGAAATATGTGAGCCATGA
 CAGAAAGGTCAAGGAGATAAAAGAAATTAGTGCACATGAGAGGTACTCCTCA
 GGTGTTAGGAAAGAGGGTAGAGCAAACCAAGGTTCCACCATATGTTGGA
 TAGGGGTCAAGTAAATTCTACTTAAACAAACAGGGCTGGGCC
 CGGTGGCTATGCCGTAAATCCCGACTTGGGAGGCTGAGGAGGGCGGA
 TCACAAGGTCAAGAGATTGAGACATCCTGGCAACACGGTAAACCGTG
 TCTCCACTAAAAATACAAAATTAGTGGCATGGTGTGCGTGCCTTA
 TTCCCAGCTACTCGGGAGGCTGAGGAGGAATCGCTTGAACCTGGGAG
 GTGGAGGTTGCACTGGGCCAGATCGCACCCTGCAATCCAGAGCGAGAC
 TGTGCAAAAAAAAAAAAAAGAAAATTCCAACAGGATGACCCCTAAG
 CCTGCAGGACTTGGAGACATCTAGGTGACTGATACTCAGTCACAAACAT
 AATTGGTCACAGCCTGATGAAATGCAAGCAGACCTTCAGATGGTATGC
 ACTCAAGTGAATCCACAAGTCCACCTAAAGAAATGCTATATTCAAGACAT
 TTGGCATCAATCTCTATCAAACAAAGATAGTCAAAGCAATGGGTTCCAA
 AAACACTTCTAAGACAATTCTCTATTGCTTTAATATCAGTCATCC
 CAGCCCTGGAAATAGAGGAGCAATGATACAGTGGTACCCCTACACAAAT
 GCACCAAGGTATTATACTCTCATGCTCCATTCTCCCTCTGCTACATC
 ACTAATAACTCATTGATTCTGGCAAGGCTCAGAGTAGGTATCGAGGATAAAAT
 ACTCTGTACCTGGAGCAAGTTGCTCAGAGTAGGTATCGAGGATAAAAT
 TTGGAAAGTTAGAAAAGCTATTAGAAGGGAGATCCTAGTAGTTGAAAACAC
 AGCCTGGCCAAGTCATGATGCTATTCTCATCTCCCAGCCTGCTGATGTCC
 ATAGCTAAGGAAGACAATTAGGCTTGGGCTAGAGGATGGGAAAGGGCAA
 AATTACTGATGCCACAGCCCAGAGAGGTATTCTAGTAATCTGAGGGTGA
 GACCACATACTGGTTCAGGGACGTACAGTGTGACAGCTGTGAGTGGAT
 GCCTGGAGTTCTGGCGTCTCTAGCACAATGATACCTGAGACTCTTGC
 ATCATTGGGAAATAATAAAATGGGAGTGGATAGATATGAAATTATGATGGC
 AATAAGCAATCAGCTAATAGCTTCATTGATGGGACAGATTAAAGATGGCT
 GCAAATCCTTGGTCCAGGTTGGGATATAAGGCAAGCATTTGTATTGGAAAT
 GCTGATAGTCTGAGGCATGAAAAGTCCACCTGCAGTAGTGGTAGGAGGA
 ACAAGCCTCACCTTCTCAATGTGTGTGACTGCTGCTTGAATTCCCTGGG
 TGGCCAGTTCCATTCTGTGTGGTCTTGGTCCACTTGAACCTGGGTGGC
 TCTGTGATGGCTTGCACAAATGATGAGTGGAAATGATGCTGTGATCAT
 TTCCAGCCTCTCCAGCCTTAAGGAACCTGGCAACTTTTATTCTGTCCCT
 TTGAAACTTGTCTTGCACCCATCCATACAGTGTGAGAAATTCTAAG
 CTGCCCATTAAGAGGCCACATGGTGATAAATTGGGTCTACATACAG
 CCCTAGCTGCTCTAGCTGACAAACAGTAGCAACTGTGTCACCAGGCGA
 GTGAACCACTTAGGACTGTATACTCCAGCCCCAGTTGAGCAATGTGGAAAC
 AGAGTAAACCATCTCAGCTTAGCCCTGCCAAACTGCGAGAATTATGAGCA
 AAATAATCCCTAGGCTTGGGTGATTTGTTCCAGATTACTGGAACAGA
 ATTGGTACCAAGGGTGGGTGAGGTGCTACAGCAATGAAAGCTTAAGACACGTG
 ACTTTGGTTTGGGTCTGAGTGGCAGGGAACTTGGCAGGCCTCAAGGAA
 ACTTTAGGGAGGGTTGAAGCATAGTGTGAGGAAACAGTAGGGGAAGCTAG
 AGGAAAAATGATGCTGGTATGTAGTGGTGGGAAGTTAGCAAAACTCG
 CCTGATGTAATGTGGGAAATTGTAAGAAACTCAGAACGATTTAAGGCATG
 TTTTATAGGCTTTAAGAAACCTCTAGGCCAGGGCGAGTGGCTCATGTC
 TGTAATCCAGCACTTGGGAGGCTGAGGTGGCGGATCACAAGGTCAAGG
 AGATCGAGACAATCCTGGCTAACATTGTGAAACCCGTCTACTAAAC
 TACAAAAAAATTAGCCGGGCATGGTGGCGGGTGCCTGTAGTCCCAGCT
 ACTAGGGAGGCTGAGGCAGAAGAATGGCGTGAACCTGGGATGTGGATCTT
 GAAGTGAGCCCAGATTGTGCCACTGCACTCCAGCCTGGCAACAGAGTGA
 GACTCCGTCTAAACCGAAAAAAAGAAACTTCTAGGGC

FIG. 4 (59 of 61)

13/118

TGGTCCCGTGGAAAGCCTCACACATGGTACACAAAGGCTGTCTTAAAAGA
 AACGTAAGTGTGTTTTGGTTAATAAAATTGATTATAATGGATAATG
 CAAAACATTTAAAGAATTACTAGCTTACATTAGCAGATTGGATCCA
 GTGATTGTTACATTCTGGTACTGAGCCCTGAATTACTCTTGAGTAAG
 GCATTATAACAAAGCTATTGATAGTTGGGTTATAGGGTGTATGTTGAA
 GAACTACTAATGTCAAAACCAATATTCACGGTCGACAAGAGGGACATCAG
 AACTGGTAATCCTTATTACCATGACTGGCTGGACAGAATACTCAATGTAA
 TGGGATTCTGCAAATAAAGACGGGGAGATGTAAGGAGATGCCTGAA
 CATTCAACATTAATGAAAGATTCAAGAAGAAATATGTATACTAACGTGAG
 CCTTATCAAGTATATGGAAAACACAAAGTTAACCGAGATAGTAAAGCAT
 TCCACTTGCTTCAGAAGTTCTTACTATGGACCCAAATAAGTGAATTACC
 TGAGAACGGGGTCCCTGTTCTCGAAGACCCACTCTACATCAGACGT
 TTTCAACAGTTGTCAAATCCCCTACCCAAATGAGAATTAAACAGAAG
 AAGAACCTGATGACAAAGGAGCCAAAAGAACCAACCCGGCAGCAGGGC
 CATAACCACACGAATGAACTGGCCACCCAGGAATCAAGACAAACGGTCAC
 ACACAGGGACCCCGTTGAAGAAAGTGAGGCTTGTCTCCTACCAACTAC
 CTCAGGTGGACTTTCAACGGCTCAGACTATCCGCTTCAATCCACATG
 CTGCCTATATCCCAACCCCTGGACCAAGCACATCCCAGCGAAGAGCAGTG
 TAGGATACTCAGCTACCTCCCAGCAGGCTCACAGGACCCACGTCAGACA
 CACGGGTACTGAGCTGCATCGGAATCTTGTCCGTGCACTGTTGTGAATGC
 TGCGGGCTGACTGTGAGCTCTCCGTGGGAACTGGTATGGGCATGAG
 AATGTAAGTACAACCAACCTGCCAGTAGCCAAGTTCTCCACCGCT
 TTTCACAGATCGGGTAGTGGCTCCAGTTGTACCTATTTGAGTTAG
 ACCTGAAAAGAAAGCGCTAGCACAGTTGTGTTGTGGATTGCTACTTTC
 ATAGTTAACTGACCTGGCTCAGACTGACCAACTTTTCCGTGAC
 AGTCTATAGCAGTTGAAGCTGAGAATGTGCTAGGGCAAGCGTTGTCTT
 CATATGTATGAATTCTCCAGTGTAAACAACATTATCTGACCAATAGTAC
 ACACACAGACACAAGGTTAACCTGGTACTTGTAAAACATACAGTAGGTGTT
 AACTCAGTGAATAACCCAGGACTAAAGTAAGGATTATTTGGTACACCTT
 TCTTGTAGTGTCTTATCAGTGAGTTGATTCTACATTAATCAGT
 GTTTCTGACCAAGAATATTGCTGGATTCTGAAAGTACAAAAGCC
 ACATAGTTTTTTCAGAAAGGTTCAAAACTCTAAAGGATTATTTCAA
 GTATAAGTTGTTTATTCTCAATCTATGACTTGACTGGTATTAAGCT
 GCTATTGATAGTAATTAGATATTCTCATTGATATAACCTGTTTGTCTT
 TCAGCAAACAAACTAAAATGATTGTACAGACACAATGCTTATTTCTG
 TTGGTGTGCTTGTGGAAAAAGAAAGAGAGATCAGATTGTACTGTGTC
 TGTGTAGAAAGTAGACATAGGAGACTCCATTGTTGTACTAAGA
 AAAATTCTCTGCCTTGAGATGCTGTTAATCTATATAACCTTACCCCCAA
 CCTCTGCTCTCTGAAACATGTGCTGTGCTCACTCAGGGTTAAATGGATT
 AAGGGCGGTGCAAGATGTGCTTAAACAGATGCTTGAAGGCAGCATG
 CTCGTAAGAGTCATCACCACCTCCCTAATCTCAAGTACCCAGGGACACAA
 CACTGCTGAAGGCCCGAGGGACCTCTGCCTAGGAAAGCCAGGTATTGTCC
 AAGTTTCTCCCCATGTGATAGTCTGAAATATGGCCTCGTGGGAGGGGAA
 AGACCTGACCGTCCCCAGCCGACACCCGTAAGGGTCTGTGCTGAGGA
 GGATTAGTATACGAGGAAGGAAACGCCCTTGCAGTTGAGACAAGAGGAA
 GGCATCTGTCTCTGCCCTGGCAATGGAATGTCTCGGTATAAAA
 CCCGATTTATGTTCCATCTACTGAGATAGGGAAAACCACCTTAGGGCT
 GGAGGTGGGACATGCGCAGCAACTGCTTTAAGACATTGAGATGTT
 TATGTGTATGCATATCTAAAGCACAGCACTTAACTCTTACCTGTCTAT
 GTTGCAGAGACCTTGTTCACGTGTTATCTGCTGACCTCTCTCCACTA
 TTATCCTATGACCCCTGCCACATCCCCCTCCGAGAAAACACCAAGAATG
 ATCAATAAAACTAAGGGAACTCAGAGGCCGGGATCCTCCATATACT
 GAACGCTTGTCCCCCTGGGCCCCCTTATTTCTCTATACCTGGTCTCT
 GTGCTTTCTTCTCAAGTCCTCGTCCACCTAATGAGAAACACCA
 CAGGTGTAAGGGCAACCCACCCCTCATTGCTGATTTGTGAGCGTGCT
 TTAAGGTAAAAAGCATGAATGTTAACCTCTTAAAGGTACAGCAGC
 CAATTCAAATATTTGTCTGATTTAATGCTAGTTGATGAGTGTCT
 TAAAATTGTTCAACATGGACACAGAGAGGGGAAACAACACATACCA
 CCTGTTGCCGGTGGGGATGAGGGAGGGAACTTAGAGGACAGGTGAACA
 GGTGCAGCAGATCACCACATGGCCACATACCTATTAACAAACCTGCAC

FIG. 4 (60 of 61)

114/118

GTTCTGCACACGTATCCCATTCTTTTTTTAAGAAATAGAAAAAAA
AATAAAATTTGTCAGTCTTCCATTAAAACCTGTTGCATGTG
GTTTAGGATGCCCTTACTCAGCAAAGGAGAAGGAATAGGAGGGCTTAG
AATTTTGAGGGAAAAAACCTATAACATAACATTGTACTGTATCAAAC
ATTTTACATGAATGACACAAGTATTCTGAATTTAAATAATTGAAACATT
GTTAAGAACAAAGGTGTCACTGAATTATTTTCATAAAATAAAATTAT
AGGGCTTAGACTGAAAGGAACAGAGAATTAAAAAATTAAAAAGAACCC
TTAGTAATTTTGATATAGTTCCATGTGCCATATTGCCATAATTGG
ATGAGAATTTTGACCTCTGGCAGGGTGACCCATATTTCANTNTATA
AAGCGTGCATCATACC

MV1KCIPPGDSQCAP;IVRYTALGHATQRVSSDQQIIPIQI.WECIRKTEAWHIIIIILNISI.QPGCPCSI.SNKCI.SSI.QRSASA
EKGSPILI.GVSKGEFCI.YCDKDKGQSIIPSI.QLKEKI.MKI.AAQKESARRPFYRAQVGSWNMLESAAIIPGWFICRSCNCN
HPVGIXNXVDIJI.GKAQKRGTCSE

FIG. 5

1	M A L E C H P D G D S N C A P G W R M T A L G H A T Q R W S S Q D Q H P Q L W E	40					T77-procutes
1	N S F - - - V G E N - - - S G W K M G S E D O - - - - - W E X D F Q D P Q	30					T77
41	C I R K T E A W H H P H L H H S L Q P G P C S - - - I S N E C L S L Q R	20	50	60	70	80	T77-procutes
25	C L E D P A G - - - - - S D L E P G P S L P T H N F M H T K T P A L A S	10					T77
77	S - - A S A E K P E G ; P E T L A G W S K G E F C L V C O E G Q S H P S L Q L K	0	90	100	110	120	T77-procutes
57	S L S A S A E K P E G ; P E T L A G W S K G E F C L V C O E G Q S H P S L Q L K	-					T77
114	E P L W E 1 A B Q E E P F T F H F A Q V G S S W H M L E S A A H P G W F	10					T77-procutes
97	X E P L W E 1 A B Q E E P F T F H F A Q V G S S W H M L E S A A H P G W F	-					T77
153	I C T - S C W C N E P W G I I N V D O - - - - - F D L O G E K A Q R G T G -	20					T77-procutes
137	I I T S C N C N E P W G I I N V D O - - - - - F D L O G E K A Q R G T G -	10					T77
184	S E	0					
177	S D	0					

117/118

FIG. 6

1	M E I - C F G U R S H L I T I L L F I F H S E T T I C R P S G R K S S K M Q A F R	IL1RA-human
1	M Y L K C H P P G D S Q C A P G Y - - - R V T A L G H A T Q R Y S S D Q Q H P Q	T77-procutes
1	A P V - F S S I N C T I - - - - - R D S Q Q K R S I V M S G - -	IL1b-human
40	I W O V N Q R T F Y I R N N Q I Y A G Y L Q G P N - W N L E E K - - - - - I D	IL1RA-human
38	L V E C I R K T E A V H H P H I L N H S L Q P G G P C S L S N K C L S S I Q R S	T77-procutes
23	- - P Y E I R E A L H I Q G Q D N E Q Q V V F S M S F V Q G E E S - - - - - N D	IL1b-human
50	V Y P I E P H A I F I G I H G G K M C L S C W K S G D E - - T R L Q I E A Y N T	IL1RA-human
73	A S A E K G S P I L G Y S K G E F C L Y C D K D K Q S H P S L Q I K E X I W	T77-procutes
78	K I P V A - - - - - L G I K E K N I Y L S C Y I K D D K - - P T L O E S V D O P	IL1b-human
55		
90		
100		
110		
120		
130		
140		
150		
160		
170		
180		
151	E A D Q P V S I T M P D E G V M V I L K E Y F Q - E D E	IL1RA-human
158	N C R E P V G I R I V D F D I L G K A Q K R G T G S E	T77-procutes
127	A E R M P W F I L G G - T K G B Q D I T D E T M O F V S S	IL1b-human

118 / 118

FIG. 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/16102

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C07H 21/02, 21/04, 1/00, 14/00, 17/00; C12Q 1/68; G01N 33/53

US CL : 536/23.1; 530/350, 387.1; 435/6, 7.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 530/350, 387.1; 435/6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG: MEDLINE, USPATFUL, WPI, BIOSIS. Search terms include author, "TANGO" and protein

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database Medline on Dialog, US National Library of Medicine, (Bethesda, MD, USA) AN 09370320. SONNENFELD et al. 'The Drosophila tango gene encodes a bHLH-PAS protein that is orthologous to mammalian Arnt and controls CNS midline and tracheal development'. Development. November 1997, volume 124, number 22, pages 4571-82, Abstract.	1-22

Further documents are listed in the continuation of Box C.

See patent family annex.

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"A"	document member of the same patent family
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"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

21 OCTOBER 1998

Date of mailing of the international search report

30 OCT 1998

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